Archives of Dermatology and Syphilology

VOLUME 38 SEPTEMBER 1938 NUMBER 3

COPYRIGHT, 1938, BY THE AMERICAN MEDICAL ASSOCIATION

VALUE AND LIMITATIONS OF BIOPSY IN DERMATOLOGY

HAMILTON MONTGOMERY, M.D.
ROCHESTER, MINN.

Histologic study of the skin is of value not only in the diagnosis but in the prognosis and treatment of many diseases.[1] Like any other single diagnostic procedure, it is far from infallible. One should be able to make a correct diagnosis from histologic examination of a cutaneous neoplasm in at least 90 per cent of cases, but the histologic picture of many inflammatory dermatoses is suggestive without being pathognomonic. To identify and to distinguish between many cutaneous diseases, observation of minute histologic changes is important; this often necessitates the study of many sections and the use of differential stains. The value of histologic study frequently has been minimized by the habit of assigning selection of the site for removal of material for biopsy to a novice rather than to a trained dermatologist. The pathologist who is confronted at necropsy with the problem of determining whether or not a lesion of early or atypical pulmonary tuberculosis is present selects the sites for the taking of specimens himself rather than leaving this selection to an inexperienced assistant. Likewise, the dermatologist should select the site for removal of tissue from a muscle (in cases of dermatomyositis and of scleroderma) or of a gland (in cases of granuloma and of neoplasm).

I wish to discuss briefly the indications for biopsy and the sites for removal of material and the technic, the fixatives and the stains to be employed. Space prevents detailed consideration of the value of biopsy in investigative studies in dermatology. In order to study the pathogenesis and the histologic changes of any dermatosis, specimens for biopsy should be obtained from lesions in different stages of development and involution, and when indicated, physiochemical and bacteriologic studies of the skin and the blood should be made at the same time.

From the Section on Dermatology and Syphilology, the Mayo Clinic.

1. Jacob, F. M., and Helmbold, T. R.: Indication for and Limitations of Biopsy in About Five Hundred Dermatologic Cases, J. A. M. A. **97**:987-991 (Oct. 3) 1931.

INDICATIONS FOR BIOPSY

Biopsy is indicated if there is any doubt regarding the clinical diagnosis of a cutaneous neoplasm, and certainly it is essential if a malignant epithelial neoplasm has recurred after treatment. For example, one cannot distinguish clinically (macroscopically) with any certainty between a basal cell and a squamous cell epithelioma. A good prognosis and cure following excision may be anticipated in all but 10 per cent of cases of squamous cell epithelioma of histologic grade 1, on a basis of 1 to 4 (Broders), but successful results occur in only 10 per cent of cases in which lesions are of grade 4. The dangers of removal of a biopsy specimen from a cutaneous neoplasm have, in my experience, been greatly overemphasized. Ewing,[2] although he warned against indiscriminate biopsy, said, "The removal of a small, carefully selected portion of a readily accessible tumor seldom results in any harm." Wood [3] cited experimental evidence with regard to animals to prove that the dangers of biopsy are overestimated. This view is supported by many recent articles.[4] It is desirable to make an immediate diagnosis of neoplasm from frozen sections, but usually this is not possible in private practice. I believe there is no danger in removal of a specimen for biopsy from a cutaneous neoplasm except in cases of melanoma or of Paget's disease of the nipple associated with underlying adenocarcinoma of the breast. Such lesions should be radically excised.

The histologic pictures of precancerous dermatoses as a group are distinctive. This group includes Bowen's disease, the various forms of leukoplakia, senile keratosis and keratoses caused by arsenic, roentgen rays, radium and tar. Usually, histologic distinction between the various members of this group is impossible. The histologic changes of epithelioma adenoides cysticum, adenoma sebaceum, syringoma and cylindroma may merge with one another, but as a group they are distinct from those changes associated with other benign neoplasms, such as syringocystadenoma papilliferans, leiomyoma, xanthoma and ganglioneuroma. It is important, as regards treatment and prognosis, to distinguish between verruca senilis, keratoma senile, lentigenes, pigmented nevus, blue nevus and early melanoma. These conditions assume an atypical clinical appearance when they occur on the backs of the hands

2. Ewing, J.: The Diagnosis of Cancer, J. A. M. A. **84**:1-4 (Jan. 3) 1925.

3. Wood, F. C.: The Experimental Pathology of Cancer, J. A. M. A. **84**:4-8 (Jan. 3) 1925.

4. Hellwig, C. A.: Biopsy in Tumors, Arch. Path. **13**:607-653 (April) 1932. McGraw, A. B., and Hartman, F. N.: Present Status of the Biopsy, J. A. M. A. **101**:1205-1209 (Oct. 14) 1933.

of elderly patients.[5] The histologic changes, however, remain constant and are pathognomonic. Many other benign neoplasms or malformations of the skin, such as angioma, ectodermal defects, nevi of various types, osteoma, hydrocystoma and sebaceous and epithelial cysts, are associated with histologic pictures that are pathognomonic.

Histologic studies are often of great value in distinguishing between various types of pigmentation of the skin,[6] including Addison's disease, acanthosis nigricans, hemochromatosis and pigmentation due to silver, arsenic and other heavy metals and in determining the role played in pigmentation by vitamin C.[7] Minute histologic changes usually permit distinction between acrodermatitis chronica atrophicans, scleroderma, dermatomyositis, lichen sclerosus et atrophicus and poikiloderma. Amyloidosis, colloid milium, pseudoxanthoma elasticum, localized myxedema, radiodermatitis,[8] molluscum contagiosum, Darier's disease, granuloma pyogenicum, ordinary verrucae and xeroderma pigmentosum are associated with diagnostic histologic pictures.

A biopsy is of distinct value in diagnosis, prognosis and treatment of various forms of cutaneous tuberculosis.[9] Distinction between the epithelioid tubercle of the sarcoid type of tuberculosis and the so-called epithelioid tubercle resulting from an anergic response in leprosy, syphilis or another dermatosis usually can be made on the basis of concomitant histologic changes observed at the periphery of the lesion. The histologic pictures of other types of granuloma, such as granuloma annulare, rhinoscleroma and granuloma associated with a foreign body giant cell tumor, including paraffinoma, are almost always specific.

Histologic demonstration of the organisms in the lesions of blastomycosis, coccidioidal granuloma and torulosis often can be made easily, although, theoretically, identification of the organisms by smear and culture should be easier and more reliable. Actinomycosis, sporotrichosis, pyoderma gangraenosum and hidrosadenitis suppurativa are associated with rather characteristic pathologic changes. Other granulomatous and pyodermic conditions, such as bromoderma, lymphogranu-

---

5. Miescher, G.; Haberlin, L., and Guggenheim, L.: Ueber fleckförmige Alterspigmentierungen: Ihre Beziehungen zur melanotischen Präcancerose und zur senilen Warze, Arch. f. Dermat. u. Syph. **174**:105-125 (May) 1936.

6. Montgomery, H., and O'Leary, P. A.: Pigmentation of the Skin in Addison's Disease, Acanthosis Nigricans, and Hemochromatosis, Arch. Dermat. & Syph. **21**:970-984 (June) 1930.

7. Cornbleet, T.: Vitamin C and Pigment, Arch. Dermat. & Syph. **35**:471-479 (March) 1937.

8. Montgomery, H.: Pathologic Histology of Radiodermatitis, in MacKee, G. M.: X-Rays and Radium in the Treatment of Diseases of the Skin, Philadelphia, Lea & Febiger, 1938, chap. 24, pp. 333-362.

9. Montgomery, H.: Histopathology of Various Types of Cutaneous Tuberculosis, Arch. Dermat. & Syph. **35**:698-715 (April) 1937.

loma venereum and furunculosis, most frequently have nonspecific histopathologic pictures and reliance must be placed chiefly on clinical appearance and various laboratory findings. Marked pseudoepitheliomatous hyperplasia of the epidermis is occasionally associated with granuloma, and careful study is required to distinguish between it and squamous cell epithelioma.

Among the inflammatory dermatoses of unknown source, psoriasis and lichen planus [10] have been regarded as having specific histologic pictures. This is usually true, but psoriasis may be imitated pathologically by seborrheic eczema and by neurodermatitis; lichen planus may be simulated by subacute disseminate lupus erythematosus, by early senile keratosis and even by a recurrent secondary syphiloderm. Lupus erythematosus, either chronic or disseminate, is usually associated with pathognomonic histologic features. It is important to remember that the histologic picture of exfoliative dermatitis remains that of the original dermatosis which caused the exfoliative dermatitis.[11] This is of value in distinguishing exfoliative dermatitis originating from a benign dermatosis from that resulting from lymphoblastoma, although often the type of lymphoblastoma can be determined only by hemocytologic, roentgenologic and other laboratory studies, by examination of a specimen removed from the sternum or from a lymph node and, at times, only by prolonged observation. Conversely, it is often possible to recognize mycosis fungoides by the histologic appearance, even in the early eczematoid or so-called premycotic stage of the disease, at which time the clinical diagnosis is only suspected.

It is obvious that many of the aforementioned cutaneous diseases, especially those which are typical, do not require biopsy for diagnosis. This is true of herpes zoster, of varicella and of variola, which are associated with distinctive histologic changes. Plaut [12] emphasized the histologic distinction between the cutaneous lesions of typhus and of typhoid fever. Histologic distinction between dermatitis herpetiformis, erythema multiforme and pemphigus at best is meager, and the diagnosis is determined more accurately by clinical observation, together with various bacteriologic and other laboratory studies. The parasitic diseases, such as scabies, and various types of trichophytic infection are diagnosed more readily by methods other than biopsy. Obviously, it is undesirable, as well as unnecessary, to obtain a specimen for biopsy from a lesion of erysipelas, of acute cellulitis or of thrombophlebitis, because of the danger of disseminating the process.

---

10. Highman, W. J.: The Significance of Histologic Examination of the Skin in Clinical Diagnosis, Arch. Path. **8**:360-363 (Aug.) 1929.

11. Montgomery, H.: Exfoliative Dermatosis and Malignant Erythroderma: The Value and Limitations of Histopathologic Studies, Arch. Dermat. & Syph. **27**:253-271 (Feb.) 1933.

12. Plaut, A., in discussion on Highman.[10]

The aforementioned cutaneous diseases do not represent a complete list, but they serve to indicate the wide field of dermatology and even of internal medicine in which biopsy may be of value in diagnosis.

SITES FOR BIOPSY

It is important to select a proper site for biopsy, not only with reference to the dermatosis which is thought to be present from the clinical standpoint but with regard to differential diagnosis. Thus, for example, if psoriasis is suspected, a well developed papule on an extensor surface would be chosen, whereas, if any type of atrophic dermatosis is thought to be present, a lesion that appears to have characteristics of the condition suspected should be chosen. In most instances the specimen for biopsy should be obtained from a lesion which represents a fully developed stage of the dermatosis. It is always advisable for purposes of comparison to include a portion of normal skin adjacent to the lesion. Fragments of tissue removed from the center of ulcers or sinuses usually are unsatisfactory for biopsy, because, as a rule, secondary infection may mask the process. Specimens for biopsy taken from the active, advancing border of larger lesions, such as neoplasms and granulomas of blastomycosis, tuberculosis and syphilis, are much more likely to reveal the true character of the condition than is a specimen taken from the center of the lesion. On the other hand, if demonstration of bacilli of tuberculosis or of other micro-organisms is desired, it is best to choose one of the earliest lesions present. In general, it is important to avoid taking a specimen from a region that has been given previous irradiation or recent applications of stimulating ointments. A lesion that is undergoing involution should not be chosen for biopsy.

Most patients object to the taking of a specimen for biopsy from the face. However, if a dermatosis involves the face, it is often possible to find a satisfactory lesion behind the ear, within the hair line or beneath the chin where the small scar will not be seen. Taking of a specimen for biopsy from the axillary or the inguinal region, including lymph nodes, should be avoided, when possible, if the patient has a dermatosis which necessitates the use of tub baths, because of the danger of breakdown at the site of biopsy and resulting secondary infection. Atrophic changes occur frequently in the region of the abdomen and the thigh, owing to friction of clothing, trauma, scratching of the skin or striae cutis distensae; such changes may confuse and obscure the histologic picture of the condition in question. When the diagnosis of hemochromatosis is under consideration, a specimen for biopsy should not be taken from the lower extremities, because stasis and other vascular diseases of the extremities may result in deposits of hemosiderin in

the skin of this region. In rare instances examination of more than one specimen may be necessary to diagnosis.

TECHNIC FOR BIOPSY

The small cutaneous punch often furnishes a specimen supplying sufficient information, but only if the site for biopsy is selected most carefully. An elliptic incision with a sharp, thin knife, deep enough to include some of the subcutaneous tissue (after which the edges are brought together by a few sutures), usually furnishes a much more satisfactory specimen than does the cutaneous punch. It permits a larger specimen to be removed, yet gives a better cosmetic result, because the line of incision usually can be made to correspond with the lines of cleavage of the skin. Thus, when indicated, sufficient material for histochemical, chemical and bacteriologic studies, as well as for histologic studies, can be obtained from a broad elliptic incision of the skin about 1 inch (2.5 cm.) long, which will result in a fine linear scar. Use of a cutting current is unsatisfactory, except for obtaining large specimens, because the heat generated and the electricity cause marked alteration of the tissues.

FIXATIVES AND STAINING

The ideal fixative for sections of skin remains to be discovered. From the practical standpoint, the dermatologist should use the fixatives with which he or his pathologist is familiar. For the majority of cutaneous diseases, it does not matter a great deal whether the fixative is solution of formaldehyde, Zenker's fluid, Bouin's solution, alcohol or a variation of Zenker's or of Bouin's formula. It is my practice to divide the larger specimens through the middle of the lesion and to place one half in a solution of 10 per cent solution of formaldehyde and the other half in a solution of absolute alcohol. Fixation in absolute alcohol is better for bacteriologic study, for staining of elastic tissue and for Unna's special stains, but alcohol causes considerable shrinkage of the tissue, making it unsatisfactory for that interpretation of the minute changes in shape and character of the cells which is necessary in diagnosis of different types of lymphoblastoma. It is obvious that alcohol should not be used in fixation when frozen sections are indicated for studies of fat, as in a case of xanthoma. Frozen sections are unsatisfactory for diagnosis of most dermatoses, because it is difficult to cut them sufficiently thin to permit study of minute structures or use of various special stains.

From a practical standpoint, staining of sections fixed in solution of formaldehyde with hematoxylin and eosin or of tissue fixed in Zenker's solution with eosin and methylene blue usually will give the experienced observer most of the information needed. As a rule, examination of only a few sections is necessary in establishing the diagnosis. If biopsy fails to reveal evidence of the histologic changes suspected, it is advisable to cut farther into the block and to use such special stains as are indicated. For example, Kaposi's sarcoma is distinguished,

in part, from other forms of sarcoma by the presence of deposits of hemosiderin. It is necessary to make serial sections and often wax reconstructions [13] when trying to trace the origin of an inflammatory or a neoplastic process to the epidermis or to one of the dermal appendages. Of the special stains most frequently employed, a good stain for connective tissue, such as Van Gieson's stain, and a good stain for elastic tissue, such as elastin H, acid orcein or Weigert's stain, are most useful; also, silver nitrate stain for melanin and Mallory's potassium ferrocyanide stain for hemosiderin frequently are indicated. Use of differential stains for fats in frozen sections, the dopa test for pigmentary disorders,[14] stains for *Gitterfäsern* and amyloid and various types of silver stains for nerve fibers frequently are indicated. Suitable stains for micro-organisms include methylene blue, carbolfuchsin, various modifications of the Gram stain and stains for spirochetes.[15]

Mention must be made of the use of the dark field to demonstrate histologically the presence of silver and of the histochemical demonstration of the presence of arsenic, of potassium and of calcium in the skin.[16] Spectrophotometric methods are of value in demonstration of the presence of various heavy metals.[17] Quantitative chemical determinations of the previously mentioned substances, of the various types of lipoids and of the content of sulfur in the skin may be of value in diagnosis, prognosis and treatment of various conditions.[18]

---

13. Ingels, A. E.: Epithelioma Adenoides Cysticum with Features of Syringoma, Arch. Dermat. & Syph. **32**:75-85 (July) 1935.

14. Becker, S. W.; Praver, L. L., and Thatcher, H.: An Improved (Paraffin Section) Method for the Dopa Reaction, with Considerations of the Dopa-Positive Cell, as Studied by This Method, Arch. Dermat. & Syph. **31**:190-195 (Feb.) 1935.

15. Farrier, R., and Warthin, A. S.: A Study of the Effect of p_H upon the Third Improved Warthin-Starry Method for Demonstrating Spirochaeta Pallida in Single Sections, Am. J. Syph. **14**:394-401 (July) 1930.

16. Lieber, G. D.: Physikalisch-chemische Wirkung der Röntgenstrahlen im Organismus: IV., Strahlentherapie **29**:139-151, 1928. Miescher, G.: Die Abwehrfunktionen der Haut gegenüber Licht, Verhandl. d. Kong. f. Dermat. (pt. 1) **9**:29-38, 1935.

17. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: A Study of Biopsy Material Taken from Patients Receiving Gold Sodium Thiosulphate, Arch. Dermat. & Syph. **28**:790-794 (Dec.) 1933; Clinical Spectroscopy: A Study of Biopsy Material from Patients Who Had Received Intravenous Injections of Silver Arsphenamine, ibid. **30**:433-438 (Sept.) 1934.

18. Cornbleet, T., and Struck, H. C.: Calcium Metabolism in Scleroderma, Arch. Dermat. & Syph. **35**:188-201 (Jan.) 1937. Klauder, J. V., and Brown, H.: Certain Phases of Sulfur Metabolism of the Skin, ibid. **34**:560-581 (Oct.) 1936. Montgomery, H.: Arsenic as an Etiologic Agent in Certain Types of Epithelioma: Differential Diagnosis from, and Further Studies Regarding, Superficial Epitheliomatosis and Bowen's Disease, ibid. **32**:218-236 (Aug.) 1935. Montgomery, H.,

(Footnote continued on next page)

SUMMARY AND CONCLUSIONS

The histologic picture associated with most forms of benign or malignant neoplasm of the skin and with a few of both common and rare dermatoses is characteristic or pathognomonic. If the dermatologist is dealing with an obscure condition, he considers several differential possibilities from the clinical standpoint. The histologic picture may not be characteristic of any one of these possibilities, but it is often possible to eliminate one or more of the diseases under consideration by study of the histologic picture. This requires careful selection of the site for removal of tissue and use of proper technic, fixatives and stains. Histologic, histochemical, chemical and bacteriologic studies of specimens have already proved their worth in investigation of dermatologic problems and should be used more extensively in the future than they have been in the past.

---

and Osterberg, A. E.: Xanthomatosis: Correlation of Clinical Histopathologic, and Chemical Studies of Cutaneous Xanthomas, ibid. **37**:373-402 (March) 1938. Osborne, E. D.: Microchemical Studies of Arsenic in Arsenical Dermatitis, ibid. **18**:37-49 (July) 1928. Pillsbury, D. M., and Sternberg, T. H.: Relation of Diet to Cutaneous Infection: A Study of the Influence of Varying Carbohydrate and Fat Intakes and of Fasting on Experimental Pyogenic Cutaneous Infections in Dogs, with Comparative Determinations of the Glycogen Content of the Skin and Liver, ibid. **35**:893-909 (May) 1937. Montgomery and O'Leary.[6] Kooyman, D. J.: The State and the Localization of Inorganic Salts in the Skin as Revealed by Extraction and Micro-Incineration, ibid. **32**:394-403, (Sept.) 1935.

TREATMENT OF PRURITUS ANI BY TATTOO WITH MERCURIC SULFIDE

EDWARD HOLLANDER, M.D.
Gastroenterologist, Manhattan State Hospital
NEW YORK

Itching about the anus is a symptom secondary to many disorders.[1] It may be caused by local conditions, such as anal fissures, fistulas, infected crypts, condylomas, the presence of pinworms or pediculi and hemorrhoids. Reflexly, diseases of the genito-urinary and of the gastrointestinal tract may give rise to anal itching, or the condition may be due to constitutional diseases, such as allergy, diabetes and gout. However, in most cases, anal itching occurs without these conditions, and there is a distinct clinical entity of primary pruritus ani. This essential pruritus ani has been ascribed by various investigators to bacterial or fungous infection of the skin, to irritation of mucus in the sinuses within the perianal skin and to "neurosis." Whatever the cause may be, there is no question that in pruritus ani of long standing the skin is infected with bacteria, and occasionally mycelial segments are found.

The treatment of primary pruritus ani by tattoo was suggested by the observation [2] that cutaneous syphilis did not involve portions of skin that had been tattooed red with mercuric sulfide (cinnabar). Since the mercurials are antiseptics as well as spirocheticides, tattoo of the perianal skin with mercuric sulfide was employed in a case of severe chronic pruritus ani. This resulted in the relief of the itching and the return of the skin to normal texture. Up to the present time the treatment has been used in fifteen cases, and all the patients have remained well; in two cases for over one year, in three for over six months and in ten for less than six months. Seven females and eight males have been treated. The duration of the symptoms ranged from two to seventeen years. In none of these cases was any rectal or constitutional disease found to account for the rectal itching. In five of the cases, after repeated scrapings of the fissured skin, segments of mycelium were seen on microscopic examination.

---

1. Rankin, F.; Bargen, J., and Buie, L.: The Colon, Rectum and Anus, Philadelphia, W. B. Saunders Company, 1932.

2. Belote, G. H.: Tattoo and Syphilis, Arch. Dermat. & Syph. **18**:200-209 (Aug.) 1928.

TECHNIC

The skin is lathered with liniment of soft soap and shaved. Tincture of metaphen is painted on the perineum and washed off with alcohol. Anesthesia is obtained by the injection of from 20 to 30 cc. of 1 per cent solution of procaine hydrochloride. Phenolated petrolatum is then rubbed into the skin and about the anal canal to insure antisepsis.

The cinnabar is mixed with sterile water to form a thick sirupy suspension. The instrument used is an electric tattoo machine with a speed of about three thousand vibrations a minute and a needle handle containing six sterile needles, which protrude 2 mm. from the machine.

In most cases of pruritus ani the skin beyond the perianal folds is excoriated and inflamed from scratching. However, it was found that when only the skin within the limits of these folds was tattooed the itching was relieved and the secondary traumatic lesions disappeared.

When the area is examined with a magnifying glass, small fissures are frequently found in the depths of the intertriginous folds of the corrugated perianal skin. These folds extend radially from the anal orifice for a distance varying from ¾ to 1½ inches (2 to 4 cm.), depending on the size and the obesity of the patient. There is an intertriginous line, frequently containing a fissure, extending upward in the midline of the intergluteal space, from the posterior margin of the anus. From the anterior margin of the anus, sulci about 1 inch long (2.5 cm.) are present on each side of the median raphe in the male and on the frenulum of the labia in the female. It is necessary to include these areas in the tattoo, for otherwise points of localized itching may persist in them. The tattooed area, therefore, has an elliptic shape, varying in size of its axes from 2 to 3 inches (5 to 7.5 cm.) laterally and from 3 to 4 inches (7.5 to 10 cm.) anteroposteriorly.

One half hour before the treatment the patient is given a barbiturate. With proper local infiltration, tattooing of the perianal skin is not painful. After the treatment an anesthetic antiseptic ointment containing 3 per cent oxyquinoline sulfate and 5 per cent ethyl aminobenzoate in petrolatum is applied. Liquid petrolatum and sedatives are prescribed for a few days. Desquamation of the skin occurs after the tattoo, and epithelization is complete within two or three weeks. The tattoo of the perianal skin is completed in one treatment. Occasionally the cinnabar is not deposited in small areas, and these require a second treatment. In the first two cases small zones were tattooed every two weeks over a period of six weeks to determine the area of skin that required treatment.

For tattoo to be permanent, the material must be deposited in the corium. Superficial deposits in the epidermis disappear through the gradual wearing of the corneal layer. Sections of tattooed skin show that the epidermis is normal and not pigmented.[3] The manner in which the deposit of mercuric sulfide beneath the epidermis exerts its beneficial effect in pruritus ani, whether by action on the cutaneous nerves or by an antiseptic action on cutaneous infection, is a question for further investigation. Since the deposit of the chemical in the skin remains for many years, the relief of symptoms should be expected to continue. That desquamation of the diseased skin is not a factor in relieving the condition is evidenced by the persistence, after desquamation has occurred, of the symptoms and the fissures in areas in which cinnabar is not present beneath the epidermis.

3. Shie, M. D.: Study of Tattooing and Methods of Its Removal, J. A. M. A. **90**:90-99 (Jan. 14) 1928.

SUMMARY

Fifteen patients with pruritus ani were treated by tattoo of the perianal skin with mercuric sulfide (cinnabar).

The relief of the itching and the return of the normal texture of the skin have continued in all the cases. In the first two cases treatment was completed over one year ago.

NOTE.—Since this article was submitted for publication, pruritus ani has been successfully treated in eleven additional cases.

The treatment of the skin by tattoo with cinnabar has been extended to other types of intractable perineal pruritus (pruritus vulvae and pruritus scroti) with successful results. The presentation of cases of these types will be the subject of a future communication.

1230 Park Avenue.

ACTIVE SWEAT GLANDS

A METHOD FOR THEIR STUDY

HANS MEYER BULEY, M.D.
CHAMPAIGN, ILL.

The secretion of sweat is of twofold importance: 1. The function of the sweat glands taken collectively may be considered as that of a single organ with an extensive influence on various processes in the human body. This "sweat organ" participates in the general water metabolism, acts as an excretory organ, aids in regulating the temperature of the body and has still other important functions which are not completely understood as yet, such as its influence on the carbon dioxide–combining power of the plasma (alkali reserve) and the oxygen-carbon dioxide metabolism of the skin. 2. The secretion of the sweat glands is important in the local processes of the skin itself under normal and pathologic conditions. Sweat moistens the upper layers of the epidermis and is an outstanding factor in the defense against parasites and the course of all chemical reactions at the surface of the skin and within the upper layers of the epidermis.

While the relationships between the secretion of sweat and general manifestations in the body have been rather thoroughly investigated, the local influence of the sweat on the processes in the epidermis and on the surface of the skin is for the most part surmised rather than actually known. Changes in the hydrogen ion concentration (p_H) of the sweat under various temporary and local conditions, particularly, offer a new field for study. The results of previous investigations of the problem have at times been discordant and even contradictory. Methods of investigation have been too crude for the subtle processes which they have been called on to examine. Evaporation and secondary contamination have definitely affected the outcome of these experiments. Previous careful investigators have succeeded only in finding average values for the entire surface of the body or a large part of it. The problem of investigating an essential point, namely, the influence of the secretion of a single gland on its surrounding terrain, has had little attention. In addition, the human subjects of previous experiments were examined under circumstances which cannot be accepted as a wholly satisfactory norm for such experiments.

From the Department of Dermatology and Syphilology, School of Medicine, University of Pennsylvania, John H. Stokes, M.D., Director.

The importance of limiting the investigation of sweat to the most narrowly circumscribed areas is emphasized by the normal anatomy of the sudoral apparatus. It is a well known fact that two kinds of sweat glands are distinguished: the eccrine and the apocrine glands. Though the types are similarly constructed, they have a different phylogenesis, the eccrine glands arising from the epidermis and the apocrine glands from the hair anlagen. The apocrine glands, located only on certain regions of the surface of the body, do not develop before puberty. The eccrine glands are distributed over the entire body, though they vary in number and size in different regions of the skin. Therefore, one may expect differences in function of the sweat glands at various sites—a "chemical geography" on and in the epidermis—and investigations which do not take account of this may lose a great deal of their value.

The results of experiments involving the production of sudoral secretion by artificial means may be misleading because of certain technical elements. Normally, the amount of sweat appearing in the pores is so small that it can be accurately observed only under the microscope or with a magnifying lens. The discharge of sweat, however, may be increased in various ways: (1) by muscular exercise, (2) by intensive mental work, (3) by thermal influence and (4) by drugs. The conditions produced in the body by these methods cannot be considered as identical with the normal state, since an increased production of sweat is associated with definite changes in the chemical constitution of the fluid. The chemical reaction of the sweat varies with each of the mentioned methods of stimulation, and it is exceedingly difficult to obtain constant conditions during the experiment itself when the production of sweat is artificially increased. The body tends to return to its normal equilibrium as soon as the irritation ceases; every subject reacts to the stimulant in a different way, and by-products, which are specific for the kind of stimulation and which may be excreted through the sweat glands, may influence the results of the experiment.

Consequently, four fundamental principles must be considered when the secretion and the chemical composition of sweat and its influence on the skin are to be investigated: 1. The examination should be confined to small, circumscribed areas—limited to a single sweat gland, if possible. 2. Contamination of the fluid with substances on the cutaneous surface and on the apparatus employed must be avoided. 3. Evaporation must be prevented. 4. The constancy of the experimental conditions must be maintained.

The only method fulfilling these requirements is that of catheterizing single sweat glands, which Yen [1] and Takahara [2] claimed to have accom-

1. Yen, T. J.: A New Method for the Measurement of the Secretion of a Single Sweat Gland, M. J. South Manchuria **12**:507, 1924; cited by Kuno, Y.: Physiology of Human Perspiration, London, J. & A. Churchill, Ltd., 1934.

(Footnotes continued on next page)

plished. They used capillary glass tubes, about 0.03 mm. in diameter at the point, introducing the tip of the capillary by means of a magnifying lens into the mouth of a duct, where it remained without support. After the larger, free end of the capillary had been filled with sweat, apparently to prevent evaporation from the freshly secreted fluid which was to be examined, the authors determined the discharged amount by calibrations of the capacity of the glass tube. In addition, the movements of the meniscus of the sweat column in the capillary were recorded by optical projection which magnified the actual movements about 160 times.

Our attempts to employ catheterization, because of its seemingly ideal features, were unsuccessful both with the originally described form of the experiment and with modified technics. While it was found to be rather easy to produce capillary tubes of the required size from glass or quartz, it was exceedingly difficult to introduce the point of the capillary into the opening of the excretory duct of the Caucasian skin, regardless of whether a binocular microscope, a magnifying lens or the naked eye was used. On the fingertips, where the experiment can be performed most easily, each mouth of the duct lies in a funnel-shaped depression in which, under certain conditions, the drop of sweat appears. This is the only moment in the experiment at which the mouth of the duct is actually visible. As the expulsion of the drop occurs rapidly, there is not sufficient time to insert the capillary tube into the opening under visual control. There is no mechanical or optical means of determining whether or not the point of the capillary, introduced between discharges of sweat, has been inserted into the duct without lacerating its walls.

A small amount of sweat, nevertheless, usually enters the glass tube after its introduction, so that it must be assumed that the capillary has reached the desired place. The only additional manipulation is that of watching with a microscope or lens to see whether or not the column in the catheter rises. Despite many experiments, each of which lasted from ten to thirty minutes, usually fifteen minutes, no rise of the column of sweat could be seen in the capillary. Occasionally no sweat at all was obtained. This occurrence was explained by the belief that the tube had perforated the wall of the excretory duct, although the subject felt no difference in the sensation caused by the introduction of the capillary. Whether the glass tube was inserted manually or with a special microapplicator (as used and described by Richards [3] for catheterization of renal glomeruli), the results were the same and were regarded as failures.

---

2. Takahara, K.: Features of the Discharge of Sweat from a Single Sweat Gland, read before the Congress of the Japanese Physiological Association, 1934; cited by Kuno, Y.: Physiology of Human Perspiration, London, J. & A. Churchill, Ltd., 1934.

3. Richards, A. N.: A Simple Instrument for Micromanipulations, J. Biol. Chem. **87**:463, 1930.

These failures may be explained by the fact that the course of the excretory ducts within the epidermis resemble a cork screw. The turns of the spiral are delicate, so that the weight of the glass or quartz tube may be sufficient to press the first coil down and thus to block any further expulsion of sweat. Another explanation of failure to get secretion of sweat may be that the cells in the wall of a secretory duct possess muscular qualities which enable them to produce a spastic contraction of the duct when mechanically irritated. Whatever the reason for the failure may be, catheterization cannot be used for routine examination of a great number of patients.

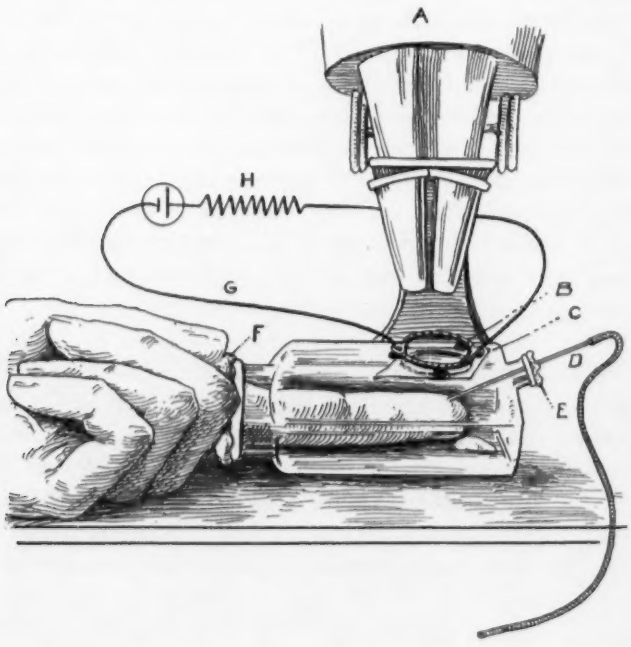
Though it was impossible to obtain the sweat directly from a single gland by catheterization, an effort was made to collect the fluid by another method, which excluded the aforementioned sources of error as much as possible. When the droplets are drawn in the capillary immediately after they have left the duct and appear on the surface as small shimmering pearls and before they spread over the skin, contamination with other soluble substances from the surface cannot be completely eliminated, but it is definitely lessened. In order to avoid evaporation, the drops may be collected in a chamber saturated with aqueous vapor. The area from which the sweat is to be collected can be chosen arbitrarily.

For this experiment a small glass chamber has been constructed which accommodates a finger and segregates it from the surrounding atmosphere, while at the same time permitting the manipulations necessary for the collection of the sweat.

A cylindric glass bottle about the length of a finger, with an opening wide enough to admit a finger without producing congestion, is flattened at two opposite planes, one of which serves as the base of the instrument. A circular opening is cut in the upper plane, over which an ordinary cover glass is kept tightly in place with wax. The investigator is thus enabled to observe the manipulations in the bottle and the production of sweat of the finger by means of a microscope. Opposite the neck of the bottle and to the side of the observation window at the end of the upper surface another smaller opening with a short neck is provided, through which capillary glass or quartz tubes are introduced, and the opening is then sealed with modeling clay. The chamber is charged with a few drops of water, in order to accelerate saturation with aqueous vapor. A small ring of insulating material, on which a fine uninsulated resistance wire is wound, is attached to the top of the cover slip by Rokitansky compound and a weak current of electricity passed through it. The heat thus produced prevents the condensation of water vapor under the cover slip and permits unhindered observation with the microscope (fig.).

This device, though far from being ideal for studying the secretion of sweat, makes a number of interesting observations possible. Artificial production of the secretion of sweat is unnecessary. All the experiments with this glass chamber were performed during the winter in a normally heated laboratory, and neither drugs nor local stimulation with heat preceded them. The circular heater on top of the cover slip was too small to raise the temperature in the chamber above that of the body.

Before the collection of sweat in capillary tubes was attempted, the mechanism for expulsion of sweat was observed. Evaporation, which



Moist chamber for the study of secretion of sweat: *A*, dissecting microscope; *B*, warming coil; *C*, observation window, sealed with microscopic cover glass; *D*, capillary pipet; *E*, clay plug in operation opening; *F*, modeling clay seal for the neck of chamber; *G*, electric circuit with battery, and *H*, rheostat.

in such observations may cause misunderstandings and failures, was excluded. Shortly after the finger had been introduced into the chamber, the skin was dried with a sponge applicator through the operation opening, after the condensation water on the inside of the glass walls showed that the air in the chamber was saturated with aqueous vapor. The effect of the sponge applicator, which should be controlled, was not studied in these experiments. Microscopic observations revealed that droplets of sweat soon appeared in several pores, while in others only

a tiny amount became visible and disappeared again in the duct without moistening the surrounding skin. A little later the same drops, this time of maximum size, returned to the surface, persisted for a short while as spherical pearls and finally spread over the surrounding surface. The entire process occurred so rapidly that many repeated observations were necessary in order that the correct impression might be obtained. When the surface of the skin was completely moistened, it was touched and dried by a cotton-tipped applicator while the chamber remained tightly closed. The stratum corneum of the skin appeared swollen, and the drops of sweat were being discharged less frequently than they had been at the beginning of the experiment. The calottes of the pearls of sweat appeared and disappeared in the pores twice and even three times before a full-sized drop was finally expelled. Nevertheless, the surface was soon covered with fluid, although it never happened that large drops of sweat ran down over the skin to the bottom of the chamber.

The mechanism of the discharge of sweat, therefore, seems to be as follows: 1. The drops of sweat are expelled by possible peristaltic contractions of duct cells. 2. The quantity of sweat must reach a certain amount before it can be expressed. In addition, two conclusions may be drawn: 1. After the expulsion, the drops of sweat remain for a short while as globules above the pores but are soon spread over the surface. 2. Apparently there are local relationships between the production of sweat and the moisture of the surface and the uppermost layers of the epidermis, which are independent of the regulation of heat in the body and which may inhibit further production of sweat.

It is not clear just where the peristaltic movement is performed in the tube of the gland. Anatomically, special cells, to which muscular abilities are attributed, are known to occur only in the coil of the gland. Whether the cells of the duct are capable of contractibility and whether such contractions are comparable to the autonomously regulated contractions of cardiac muscle cells is unknown, although a circular arrangement of epithelial fibers around the excretory canals has been found by polarized light.[4] The duct cells within the upper layers of the epidermis are probably deprived of any motility by mechanical considerations. The stiff corneal layer probably hinders such movements. Even though only the secretory part of the gland is able to produce peristaltic contractions, the discharge of sweat may be thought of as the result of peristalsis.

4. von Ebner, V. Koelliker: Handbuch der Gewebelehre des Menschen, 1902, vol. 3; cited by Pernkopf, E., and Patzelt, V.: Anatomy and Histology of the Skin, in Arzt, L., and Zieler, K.: Die Haut- und Geschlechtskrankheiten, Berlin, Urban & Schwarzenberg, 1934, vol. 1, p. 42.

The Manchurian physiologist, Kuno, who observed the discharge of sweat simply with a microscope, described and explained the process in his monograph [5] on human perspiration, as follows (p. 215):

> The discharged sweat drops look like glittering pearls, but soon disappear from view, probably because they spread away over the skin. In each sweat pore the discharge takes place periodically at irregular intervals and not continuously.

My findings confirm his statement, though the experiments with the glass chamber reveal that the disappearance of the pearls of sweat from view is due not only to the spreading and evaporation but to the sucking backward movement, or reaspiration, of drops too small to be expelled by the peristalsis of the glandular ducts.

Kuno's opinion as to whether the periodic discharge is due to the type of cellular contractions in the duct or to periodic secretion in the secretory portion of the gland is not clear. At one point (p. 218), he stated:

> The question of how the periodical discharges of sweat result, cannot be answered definitely. But it seems more probable that they are due to periodical contractions of the muscular fibers of the sweat glands than that they are due to periodical secretions of sweat. . . .

Later he corrected his previous statement by writing:

> That the discharges of sweat take place at irregular intervals and independently in individual sweat glands may be explained on the assumption that the muscular contractions are elicited whenever sweat is accumulated to a certain amount in the lumen of the sweat gland. The frequency of the muscular contractions may then depend upon the rate of sweat secretion and the discharge of sweat may take place more frequently in sweat glands with strong activity than in others.

Obviously, the production of sweat and the expulsive contractions cannot be separated. The rate of discharge certainly depends on the amount of sweat produced. The peristalsis influences the discharge only to the extent that too small an amount of fluid cannot be expelled and that therefore the size of the discharged drops is rather uniform. The experiments with the glass chamber revealed these processes definitely.

It is more difficult to explain why the rate of production and discharge of sweat decreases when the content of water in the uppermost layers of the epidermis reaches a certain point. Saito,[6] who studied the action of the sweat glands of the soles in cats after cutting the sciatic nerve, showed in his experiments that, in addition to central nervous regulation, there are local factors creating impulses of stimulation and

5. Kuno, Y.: Physiology of Human Perspiration, London, J. & A. Churchill, Ltd., 1934.

6. Saito, K.: Mechanism of Sweat Secretion from Foot of Cat, J. Orient. Med. **11**:39, 1929.

suppression to the secretory cells in the sweat glands. However, there are no known facts which may be able to give an approximate understanding of the actual occurrences. It is not impossible that the cells of the sweat ducts conduct the stimuli from the stratum corneum downward to the secretory cells.

For chemical examination, sweat may be collected within the glass chamber by means of capillary tubes which are operated through the small opening lateral to the observation window ("operation opening"). The plastic compound covering this hole permits sufficient mobility of the capillary tube without leakage of air. In order to avoid evaporation through the catheter, its outer end may be connected with a closed water bottle by thin rubber tubing. The drops of sweat can then be picked up as soon as they become visible in the pores. The liquid rises in the tube by capillarity. To avoid contamination of the fluid from prolonged contact with the cutaneous surface, the tube should be repeatedly dried of superfluous sweat, and thus a sufficient quantity of liquid of comparatively great purity may be obtained for micro-analytic studies.

The drops of sweat must be collected rather rapidly because of the cessation or, at least, diminution in the amount of sweat discharged when the corneal layer of the epidermis is saturated with water; otherwise the finger must be removed from the chamber and dried in warm air before the collection of sweat is resumed. This interruption, however, ought to be avoided, for it might influence the result of the experiment, since the smallest changes or mistakes in the experiment cause great errors in the micro-analytic measurements.

An interesting study would be the determination of the quantity of sweat produced by a single gland under various conditions and in different regions. A portion of the fluid, however, is probably resorbed while passing the stratum corneum, since keratin is a hygroscopic substance readily adsorbing sweat, which in turn supports the process of keratinization by its acid reaction. The facts that in histologic sections the corneal cells in the environs of the sweat ducts appear to be lighter stained and more swollen than horn cells in other sites and that keratinization occurs farther below around the ducts, corroborate this theory. Since it is unknown how much sweat invades the corneal layer through the walls of the ducts, a quantitative determination of the amount of sweat discharged on the surface is of only relative accuracy.

The simplest way to determine the quantity of sweat secreted by a single gland is to calibrate the capillary glass tube containing one drop of sweat by means of a microscope. Because of the uniformity in the size of the drops, the amount of sweat discharged on the surface may be obtained by counting the number of expelled drops and multiplying this number by the volume of the single drop.

SUMMARY

1. Previous studies of the secretion of the sweat have been rather gross and have involved the use of artificial means of production of sweat.

2. The ideal technic for examination of sweat would involve (*a*) examination of a single gland, (*b*) avoidance of contamination with substances on the cutaneous surface, (*c*) exclusion of evaporation and (*d*) constancy of the experimental conditions.

3. The method of catheterization proposed by Yen and Takahara seems theoretically to fulfil these requirements for an ideal technic but has failed in our hands.

4. Therefore, a new apparatus for observing the secretion of sweat and collecting the fluid has been constructed. This consists essentially of a chamber which encloses the area to be observed and which permits the manipulation of capillary tubes without artificial means for stimulation of sweat.

5. By the use of this apparatus it has been possible to observe the mechanism of discharge of sweat and to estimate the production of sweat of a single gland.

Drs. A. N. Richards and H. C. Bazett made valuable suggestions for the construction of the apparatus described.

DERMATITIS AND STOMATITIS FROM THE MERCURY OF AMALGAM FILLINGS

EUGENE F. TRAUB, M.D.

AND

ROY HERBERT HOLMES, M.D.

NEW YORK

Reported instances of dermatitis or stomatitis from the mercury of amalgam fillings are rare, but undoubtedly such cases occur more frequently than a review of the literature would indicate. We have recently observed 2 examples of such a dermatitis, and we believe they are the first to be recorded in this country. In our first patient a mild stomatitis was also present. In neither of our patients was the cause recognized at the time of the first attack, and no doubt in many cases a mild involvement is unrecognized. We desire to stress the point that such cases represent examples of contact dermatitis rather than of irritation of the skin and the mucosa resulting from the absorption of mercury from the amalgam fillings and to review briefly the literature on the controversial subject of chronic mercurial poisoning resulting from amalgam fillings.

REPORT OF CASES

CASE 1.—J. L., a schoolgirl aged 13, born in the United States, first came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 10, 1937, because of dermatitis venenata. The patient had had eczema on and off for five years and in 1930 a violent reaction had developed after an injection of diphtheria antitoxin. The hives and edema at the time were so severe that she had been more or less confined to bed for two months. The first attack similar to the current trouble had occurred five years before and followed the filling of teeth with amalgam. She had had three successive similar attacks, the most recent of which began five days before admission, when she had some dental work done which did not involve the use of any injection (such as procaine hydrochloride). Amalgam fillings were placed in several of her teeth in the morning, and that afternoon she noticed a slight redness on the chin and on the right side of the angle of the mouth. Olive oil was used to clean the skin, and a zinc salve was applied. When these gave no relief, spirit of camphor was applied locally. As the condition did not get better, she went to her physician, who prescribed 5 per cent ammoniated mercury ointment. When no improvement was noted, the strength of the ointment was increased to 10 per cent. This merely increased the severity and spread of the eruption. She therefore came to the hospital for treatment. Examination revealed a mild stomatitis extending down

From the Skin and Cancer Unit, the New York Post-Graduate Medical School, Columbia University.

toward the right molar region and a slight cheilitis. On the cutaneous surface the eruption involved the chin, extending down the left side of the neck anteriorly, with slight irritation on the upper part of the left arm, the chest and the neck. The eruption was patchy, with sharply outlined borders, erythematovesicular and slightly hot to the touch. There were many tiny vesicles, some of which were tense and closely packed. The older lesions showed some crusting. There was mild edema of the right upper eyelid. Wet dressings of boric acid were prescribed, and in a week the eruption practically subsided. There were no general systemic symptoms and no evidence of generalized mercurial poisoning. An examination of the urine for mercury was not made.

Patch tests with the following substances were performed, with the results noted: 10 per cent coal tar, indefinite; 10 per cent sulfur ointment, 1 plus; 5 per cent ammoniated mercury in 5 per cent salicylic acid, 3 plus; 10 per cent salicylic acid, 3 plus; benzoic acid, 1 plus; juniper tar, 1 plus; 2 per cent mercurochrome, 4 plus; 10 per cent peruvian balsam, 1 plus; 10 per cent ammoniated mercury, 4 plus; 1 per cent nupercaine-Ciba, 3 plus; 1 per cent menthol, 2 plus; 1 per cent thymol, 1 plus; boric acid ointment, 1 plus; rectified oil of birchtar, 2 plus; butesin picrate, indefinite; 0.91 per cent aqueous solution of sodium arsenate, 1 plus (erythema); butesin picrate (as made), 3 plus (vesicular erythema, edema); 1:1,000 aqueous solution of mercuric chloride, 4 plus (bullous with erythema, edema). All other chemicals gave negative results. A Prausnitz-Küstner test was not done.

Case 2.—R. J., a woman aged 27, presented moderately severe dermatitis venenata about the mouth, the face and the neck after the insertion of an amalgam dental filling. This patient had had a previous similar attack. Both attacks were mild and were not aggravated by any further application of mercury. In each instance the dermatitis, which had appeared suddenly after the filling of her teeth with amalgam, cleared rapidly in about one week with soothing applications. We were not given an opportunity to study this patient by patch tests or other laboratory procedures.

The preparation for the application of an amalgam filling consists in combining a powdery mixture of copper, silver, tin and zinc with pure mercury, to form a plastic mass. This is either stirred in a mortar for about three minutes or mixed in the palm of one hand, the fingers of the other hand being used for kneading. Regardless of which method is followed, considerable mercury generally adheres to the dentist's hands, and this in turn is rubbed on the patient's skin around the mouth, producing direct contact. In those cases in which acute dermatitis or stomatitis occurs, the process is undoubtedly due to contact rather than to the absorption of mercury, as intimated in some of the reported cases. When the dentist attempts to press or squeeze out any excess of mercury while kneading the material into the cavity, the patient probably swallows a few fine particles in many instances. The mercury taken into the gastrointestinal tract in this way is undoubtedly eliminated in a large measure, if not entirely, without being absorbed by the body. The dermatitis or stomatitis which occurs after the insertion of an amalgam filling takes place immediately, i. e., within a few hours, and is localized to those areas which are in contact with the

dentist's hands while he is working. It seems to us, therefore, that in cases of acute dermatitis or stomatitis, the question of absorption of mercury may be excluded.

It is worth noting that in case 1 the patient reacted strongly to the patch tests with all the mercurial preparations used in our routine test series, namely, mercuric chloride (1 : 1,000 aqueous solution), ammoniated mercury (5 per cent and 10 per cent) and mercurochrome (2 per cent). She reacted in varying degrees to a number of other chemicals. Her history of long-standing eczema of undetermined origin and of a severe reaction to serum fit into the picture of multiple sensitivity, most acute at this time to mercury. The use of ammoniated mercury ointment before we saw her made it impossible for us to determine the exact extent of the dermatitis due to the mercury in the amalgam fillings, but from the history it was apparent that the ammoniated mercury exaggerated all the symptoms and probably was responsible for the spread of the eruption down on the neck, the chest and the arm. The sensitivity to mercury in this patient extended even to the mucous membranes of the lips and the mouth, a point worth stressing because in some reported cases of high cutaneous sensitivity mercurial applications on the mucous membrane were tolerated without reaction.

Interest in this country was first focused on the possibility of chronic mercurial poisoning from amalgam fillings in teeth by a series of communications which appeared in *The Journal of the American Medical Association* from 1926 to 1928. In the first two of these, Stock [1] detailed his own case of chronic mercurial poisoning extending over from twenty to twenty-five years, and he concluded that amalgam fillings are injurious to health. Diech, Schönbeck and Schröder,[2] in a discussion of Stock's experience, said that the dangers of amalgam fillings had been known for a long time but that experiments had shown that mercury is given off only for a few days after the filling is applied and that Stock had greatly exaggerated this menace. Stock expressed the belief that amalgams were especially dangerous in the presence of other metals (gold crowns, etc.) because of the electrolytic action of the galvanic current passing between the different metals. Joachimoglu [3] pointed out that the widespread use of amalgams, really a mass experi-

1. Stock, A., (*a*) cited in The Use of Amalgam for Dental Fillings, Foreign Letter (Berlin), J. A. M. A. **87**:685 (Aug. 28) 1926; (*b*) Die Gefährlichkeit des Quecksilberdampfes und der Amalgame, Med. Klin. **22**:1250 (Aug. 13) 1926; abstracted, J. A. M. A. **87**:1599 (Nov. 6) 1926.

2. Diech, Schönbeck and Schröder, cited in The Use of Amalgam for Dental Fillings, Foreign Letter (Berlin), J. A. M. A. **87**:685 (Aug. 28) 1926.

3. Joachimoglu, cited in The Use of Amalgam for Dental Fillings, Foreign Letter (Berlin), J. A. M. A. **87**:685 (Aug. 28) 1926.

ment, indicated that they are harmless and that symptoms like those of a chronic cold are insufficient evidence of mercurial poisoning. He stated that the recovery of excessive amounts of mercury plus the symptoms of mercurial poisoning is necessary to justify such a diagnosis. Hahn and Umber [4] expressed the belief that idiosyncrasy plays a role, as large amounts used in the treatment of syphilis seldom result in poisoning.

Ritter,[5] in a series of urinalyses (using Stock's method) of persons employed in dental laboratories using the worst (copper) amalgam, found no mercury. Führer [6] stated that the existing literature gave the impression that with the elimination of a few hundredths of a milligram of mercury in the daily output of urine no signs of chronic mercurial poisoning had been observed, but that with the excretion of a few tenths of a milligram such signs had appeared.

In view of the controversial nature of the subject, His [7] in 1928 established a medical center in Berlin, Germany, where persons apparently suffering from manifestations due to amalgam fillings might be studied. Fleischmann,[8] who was in charge of the research, showed that certain persons are "mercury carriers," even though they present not the slightest evidence of mercurial poisoning. Hence, the mere demonstration of the presence of mercury is not necessarily equivalent to a diagnosis of "mercurial poisoning" The report stated:

> With difficulty, fifty-one persons were found who had had no contact with mercury other than with that which had been used in their teeth. Of these fifty-one subjects, thirty-seven had copper-amalgam fillings. In thirty of these thirty-seven subjects, or 81 per cent, the presence of mercury in the mouth, outside the fillings, was demonstrated, whereas in the fourteen subjects with pure analgam fillings there was only one in whom mercury could be so demonstrated. Even a large number of pure amalgam fillings (some subjects had as high as thirteen, or even fifteen, fillings) could be present without delivery of mercury. In eight, with poisoning due to copper-amalgam fillings, the symptoms disappeared after removal of the fillings; likewise, the eliminations of mercury ceased. Furthermore, thirty-seven school dentists and twenty-four school dental nurses were examined by Professor Fleischmann, and in nearly all there were manifestations of fatigue, a tendency to headache, and the like, while in two persons distinct symptoms of mercurial poisoning were observed. This proves that dental work that involves the application of amalgam fillings constitutes a danger.

---

4. Hahn and Umber, in discussion on Stock.[1b]

5. Ritter, in discussion on Stock.[1b]

6. Führer, cited in Chronic Mercurial Poisoning and the Menace of Amalgam, Foreign Letter (Berlin), J. A. M. A. **89**:388 (July 30) 1927.

7. His, cited in Objections to the Use of Amalgam for Filling Teeth, Foreign Letter (Berlin), J. A. M. A. **90**:1056 (March 31) 1928.

8. Fleischmann, cited in Objections to the Use of Amalgam for Filling Teeth, Foreign Letter (Berlin), J. A. M. A. **90**:1056 (March 31) 1938.

While it was conceded by Stock [9] and by Zangger, Haber and others whom he cited that copper amalgam fillings are the most dangerous, the pure amalgams vary so greatly in quality that they cannot be looked on as entirely safe. From his own experience, Stock warned that even gold fillings may contain mercury in amounts sufficient to cause symptoms.

A thorough investigation was carried out by Souder and Sweeney,[10] who concluded that there is no justification in the claim that mercury as a vapor or as a solution from standard amalgams passes into the body by way of the air or of food taken into the mouth. While no clinical controls were carried out, the authors demonstrated that an almost negligible amount of mercury vapor is given off from a definite surface of amalgam and that it is practically impossible for mercury to be dissolved in the mouth. The question of absorption of mercury through the root canal was not touched on, but the authors' experiments were rather convincing that little mercury is taken in by inhalation of vapor, through particles broken off or abraded from fillings or by the solution of mercury in the mouth. Furthermore, they found almost as frequent excretion of mercury in persons without amalgam fillings as in those with amalgam in their teeth. The thought was expressed, however, that while the amount of mercury that might be absorbed from such fillings is possibly not sufficient to produce demonstrable toxic effects in a normal person, in the hypersensitive subject there might be a pronounced reaction.

One of the few recorded cases we could find of acute mercurial dermatitis similar to ours was that noted by Blumenthal and Jaffé [11] in 1929.

The patient, a woman aged 30, after the fourth occurrence of rather severe stomatitis and acute dermatitis of the face, the neck and the shoulders, consulted the authors. It was found that the time of the attacks corresponded to the date of the prosthetic work. Patch tests with a 2.5 per cent solution of 1:250 mercury hydrochloride produced edema and vesiculation (size of a quarter in twelve hours). The authors were able successfully to prove the hypersensitivity to mercury by passive transfer. The damage in this patient occurred in the first hour after the amalgam filling was applied, which coincided with the time during which the mercury in the amalgam was present as the mercury ion.

---

9. Stock, A.: Die Gefährlichkeit des Quecksilbers und der Amalgam-Zahnfüllungen, Med. Klin. **24**:1154 (July 27) 1928; abstracted, J. A. M. A. **91**: 1070 (Oct. 6) 1928. Haber, G.: Beitrag zur Quecksilbergefahr durch Amalgamfüllungen, Deutsche Monatschr. f. Zahnh. **45**:938 (Nov. 1) 1927.

10. Souder, W., and Sweeney, W. T.: Is Mercury Poisonous in Dental Amalgam Restorations? Dental Cosmos **73**:1145 (Dec.) 1931.

11. Blumenthal, F., and Jaffé, K.: Amalgamplomben als Ursache von Quecksilberdermatitis, Deutsche med. Wchnschr. **55**:1720 (Oct. 11) 1929.

They stated:

A hardened amalgam will give practically no mercury, but fresh amalgam, which has a surplus of mercury, can for a time cause an overflow. Thus, dermatitis comes soon after the filling is put in and may subside without the taking out of the filling. Such was the case with our patient.

In a later article, Blumenthal and Jaffé [12] stated that they were not able to repeat the passive transfer of hypersensitivity to mercury. Blumenthal [13] said:

Since in many hundred cases of contact dermatitis, I was never successful in obtaining a passive transfer, I doubt the specificity of the exceptional positive result obtained in the first case. Contrary to the belief of Urbach and others, I believe that the presence of reagins in contact dermatitis is still to be demonstrated.

Meyer,[14] shortly after the report by Blumenthal and Jaffé, cited 2 cases of mercurial poisoning from amalgam fillings; a brief abstract of the report of his first case is of significance:

R. F., a woman aged 40, complained of burning of the tongue, digestive upsets, dryness of the mouth and the throat, inflammation of the gums, poor appetite, weakness and numbness of the hands and the feet, general discomfort, lack of interest, depression, disturbed sleep and loss of weight. The disproportion between the slightly abnormal physical findings and the patient's numerous complaints was striking (a point the author noted in his second case). The blood picture was atypical, with a high leukocyte count and a low percentage of hemoglobin. In the search for the cause of the symptoms, several old copper amalgam fillings were discovered and removed. Examination of the urine just prior to extraction of the teeth showed 0.004 mg. of mercury in a twenty-four hour specimen of 1.5 liters. Within a few weeks after removal of the teeth all symptoms disappeared with the exception of a slight burning of the mouth and tongue, and the patient was restored to good health.

The author expressed the belief that both his cases conclusively proved that mercurial poisoning had resulted from the amalgam fillings.

Herrenknecht and Scheidt [15] expressed the opinion that in most cases mercurial poisoning results from inhalation rather than from swallowing of any of the metallic particles, as little, if any, absorption takes place through the gastrointestinal tract. Mercury found in examinations of the stool, therefore, is of less significance than that discovered in the urine. They stressed the point (without submitting evidence to prove it) that when an amalgam filling is in contact with other metals in the

12. Blumenthal, F., and Jaffé, K.: Zur Frage der Quecksilberempfindlichkeit, Dermat. Wchnschr. **91**:1668 (Nov. 8) 1930.

13. Blumenthal, F.: Personal communication to the author, August 1937.

14. Meyer, E.: Quecksilbervergiftungen von Zahnfüllungen ausgehend, Med. Welt **4**:703 (May 17) 1930.

15. Herrenknecht, W., and Scheidt, C.: Mundhygiene, Fortschr. d. Zahnh. **6**: 664 (Aug.) 1930.

mouth, the possibility that free mercury may be released is much enhanced. In cases in which other metals were present they stated that amalgam fillings should be avoided. They expressed the opinion that up to the time of their study (August 1930) no absolutely satisfactory case of mercurial poisoning from amalgam fillings alone had been presented but admitted that in the rare examples of hypersensitivity to mercury, damage from such a source is a possibility. They concluded that as far as the patient is concerned little danger results from the use of silver amalgam and that copper amalgam should not be used, chiefly out of consideration for the safety of the dentist and his helpers (who might suffer from the inhalation of the mercury).

Sacher [16] reported an interesting case of stomatitis and acute mercurial poisoning from amalgam fillings.

> The patient was a 61 year old man. Shortly before the onset of the disease, he had had six new amalgam fillings. The illness under consideration had begun with soreness of the throat and mouth and much secretion from the nose. There were swelling of the joints, throbbing of the arms and legs, fever, malaise, irritation of the skin and albumin and casts in the urine; laboratory examinations showed no other abnormality. The patient's condition varied from better to worse for about six months, until the amalgam fillings were suspected as the cause. An examination of the urine then showed 0.04 mg. of mercury, which was considered to be ten times the content of normal urine (0.003 mg. being practically normal). All the fillings were then removed, and three teeth were extracted. The patient made an almost complete recovery in four weeks. One of the dentists stated ". . the fillings had been improperly prepared, not having the necessary cement base in the root canal."

A more recent case (that does not seem convincing to us, however) was that noted by Preininger [17] of sensitivity to nickel coins and to mercury bichloride (1:10,000):

> The patient was a 46 year old dentist with amalgam fillings, who had a professional dermatitis. He presented a dyshidrotic eruption on the hands and feet of three weeks' duration. He had spent much time making gold teeth, and only in the last year he had started using amalgam fillings. Two amalgam fillings had been put in his own teeth during the past ten years. When these were replaced with cement fillings, his cutaneous eruption regressed in two or three weeks and remained absent during four months' observation. The patch tests, which had been repeatedly positive, became rapidly negative after the irritation was stopped (removal of amalgam).

One could scarcely consider the presence of hypersensitivity on the part of the patient. The Prausnitz-Küstner reaction of this patient was negative. The questionable point in this case was the author's

16. Sacher, H.: Zwei ungewöhnliche Fälle von Schwermetallstomatitis, Ztschr. f. Hals-, Nasen- u. Ohrenh. **30**:433 (May) 1932.

17. Preininger, T.: Ueberempfindlichkeit gegen Nickelgeld, Dermat. Wchnschr. **99**:1082 (Aug. 18) 1934.

failure to explain satisfactorily the exactly similar eruption on the doctor's feet, which from his description certainly suggested a dermatomycosis. Because the author failed to exclude such a primary infection on the feet, the reasonable possibility of a dyshidrotic dermatophytid of the hands, which generally temporarily clears rather promptly with or without special treatment, cannot be excluded. In view of the possibility of such an infection, the removal of the amalgam fillings might well have been a purely coincidental factor. The rather sudden loss of cutaneous hypersensitivity to nickel and to mercury does not necessarily substantiate either point of view. It must be presumed that the dentist stopped handling the amalgam. The author did not make this point clear. In a review of the reasons for professional dermatitis in dentists, Rosenthal [18] cited solution of formaldehyde and procaine hydrochloride as the most common causes. Amalgam fillings were not mentioned as a possible causative factor.

Stock, Brüggemann, Fleischmann, Lichtwark, Werkenthin, Borinski, Führer and others cited by Sacher [16] all agreed that mercurial poisoning from amalgam fillings is possible.

In addition to the many ways already mentioned by which mercury may get into the body from amalgam fillings, Timm [19] has shown that deposits of heavy metal wander into the dental canal and the surrounding tissues and are actively present as sulfides and as sulfates and carbonates. He found that there is a flow of lymph away from the dental canal and around it.

Hawkins [20] reported the case of a 7 year old boy with a hypersensitivity to mercurochrome who also reacted strongly to ammoniated mercury ointment but tolerated applications of mercurochrome on the mucous membranes of the tonsils and oral administration of mild mercurous chloride. He stated that it is generally accepted that the skin may exhibit a hypersensitivity not shared by the mucous membrane, there being numerous recorded examples. It has been commonly observed that not every patient who is hypersensitive to one or even more mercurical preparations necessarily reacts positively to all of them.

CONCLUSIONS

From our review of the experimental work and reports of cases concerning the dangers of amalgam fillings and from our own experience in the matter, it would appear that the following conclusions are justifiable:

18. Rosenthal, S. K.: Zur Kenntnis der Berufsekzeme bei Zahnärzten, Dermat. Wchnschr. **98**:142 (Feb. 3) 1934.

19. Timm, F.: Die Wanderung von Schwermetallen in Substrate und Gewebe, Deutsche Ztschr. f. d. ges. gerichtl. Med. **24**:51, 1934.

20. Hawkins, H. F.: Mercurial Skin Sensitization, Dallas M. J. **20**:105 (Nov.) 1934.

1. The danger to the patient of chronic mercurial poisoning from silver amalgam fillings alone is remote.

2. Chronic mercurial poisoning from copper amalgam alone is not frequent and is to be expected only in subjects who are hypersensitive to the metal.

3. Acute manifestations such as dermatitis or stomatitis from amalgam fillings are probably more common than a review of the literature would indicate and simply represent a hypersensitivity to mercury externally applied.

4. The finding of mercury in the urine is of greater significance than the finding of mercury in the stool. However, as many apparently normal persons without amalgam fillings excrete mercury in the urine, the amount of mercury recovered should be pronounced (excessive) before it is regarded as of diagnostic significance.

5. The degree of sensitivity to different preparations of mercury varies in each case, nor does every patient necessarily react to all mercurial compounds. The skin generally reacts more readily to the external application of mercury than does the mucous membrane.

EXTRAGENITAL GRANULOMA INGUINALE

ROBERT B. GREENBLATT, M.D.

RICHARD TORPIN, M.D.
AND
EDGAR R. PUND, M.D.
AUGUSTA, GA.

Granuloma inguinale, as the name implies, is a granulomatous process which usually occupies the inguinal region. The well known proclivity of the disease for the external genitalia has earned for it a place in the category of venereal diseases. Its venereal origin, however, has never been absolutely proved.

The development of granuloma inguinale is not confined to the external genitalia, the vagina, the perineum, the buttocks and the groin. It may occur primarily on the cervix. The recognition of this fact is of utmost importance in the differentiation of carcinoma of the cervix uteri, which it closely simulates.[1] Recently there was recorded a case of granuloma inguinale of the uterus, tubes and ovaries.[2]

EXTRAGENITAL SITES

It has long been known that extragenital lesions occur. In 1905 Donovan [3] was struck by the granuloma-like appearance of the lesions in the mouth of a boy in a ward. Scrapings were examined, and the intracellular bodies which now bear Donovan's name were seen. One is led to believe that lesions of this disease about the mouth were not uncommon in India. Sequeira [4] in 1908 described lesions at the left angle of the mouth and on the right thigh of a Negro with granuloma inguinale tropicum. Howard Fox [5] analyzed 150 cases of granuloma

From the Departments of Pathology and Gynecology, University of Georgia School of Medicine.

1. Pund, E. R., and Greenblatt, R. B.: Granuloma Venereum of the Cervix Uteri Simulating Carcinoma, J. A. M. A. **108**:1401 (April 24) 1937.

2. Pund, E. R., and Gotcher, V. A.: Granuloma Venereum of the Uterus, Tubes and Ovaries, Surgery **3**:34 (Jan.) 1938.

3. Donovan, C.: Ulcerating Granuloma of the Pudenda, Indian M. Gaz. **40**: 414, 1905.

4. Sequeira, J. H.: A Case of Granulomatous Swellings at the Left Angle of the Mouth and in the Right Inguinal Region, Proc. Roy. Soc. Med. (Sect. Dermat.) **1**:92, 1908.

5. Fox, H.: Granuloma Inguinale: Its Occurrence in the United States, J. A. M. A. **87**:1785 (Nov. 27) 1926.

inguinale recorded in the United States up to 1926. He noted that in 9 cases a lesion occurred in a region other than the genital. In only 2 was the diagnosis confirmed microscopically. The parts affected included the cheek (Lynch [6]), the side of the neck (Ross [7]) the nose, the throat and the mouth (Ross [7]), the upper lip and the side of the neck (Parounagian and Goodman [8]), the lip, the pharynx and the larynx (Hunter [9]), the back of the hand (Claassen [10]), the side of the neck (Winfield [11]), the thigh at the site of a graft of skin (Gage [12]) and the lower lip (Taussig [13]). Since Fox's excellent review other cases of extragenital lesions have been recorded in the American literature; the affected sites, including the shoulder,[14] the larynx [15] and the mouth.[16]

INCIDENCE

Analysis of all these cases shows that extragenital granuloma inguinale occurred in about 6 per cent. Among McIntosh's [17] 15 cases was that of a Negro who had lesions in the groin, on the anus and on the neck. This case was reported in detail by Harris [15] as one of laryngeal involvement. At the University Hospital Clinic of the University of Georgia School of Medicine we have studied some 45 proved

6. Lynch, K. M.: Granuloma Inguinale, J. A. M. A. **77**:925 (Sept. 17) 1921.

7. Ross, C. F.: Granuloma Inguinale, Virginia M. Monthly **1**:401 (Sept.) 1923.

8. Parounagian, M. B., and Goodman, H.: Ulcerating Granuloma (Granuloma Inguinale): A Report of a Rare Example of This Disease in a Syphilitic Patient, Arch. Dermat. & Syph. **5**:597 (May) 1922.

9. Hunter, R. J.: Granuloma Inguinale with Associated Lesions of the Lip, Pharynx and Larynx: Report of a Case, Tr. Coll. Physicians, Philadelphia **45**:455, 1923.

10. Claassen, H. L.: Granuloma Inguinale, Ohio State M. J. **18**:685 (Oct.) 1922.

11. Winfield, J. M.: Granuloma Inguinale: Two Cases, Arch. Dermat. & Syph. **5**:832 (June) 1922.

12. Gage, I. M.: Granuloma Inguinale, Arch. Dermat. & Syph. **7**:303 (March) 1923.

13. Taussig, F. J.: Contribution to Pathology of Vulvar Diseases: C. Granuloma Inguinale, Am. J. Obst. & Gynec. **6**:411 (Oct.) 1923.

14. De Monbreun, W. A., and Goodpasture, E. W.: Etiological Studies of Granuloma Inguinale, South. M. J. **24**:588 (July) 1931.

15. Harris, R.: Granuloma Venereum: General Discussion with Report of a Case of Laryngeal Involvement, Laryngoscope **40**:707 (Oct.) 1930.

16. Sidlik, D. M.: Granuloma Inguinale of Face and Mouth, Arch. Dermat. & Syph. **15**:703 (June) 1927. Muckenfuss, R. S., and Brown, J. B.: Granuloma Inguinale, with Report of a Case with Oral Involvement, Internat. J. Orthodontia **18**:988 (Sept.) 1932. Silva, F.: Buccal Localization of Venereal Granuloma Case, Urol. & Cutan. Rev. **37**:611 (Sept.) 1933.

17. McIntosh, J. A.: Etiology of Granuloma Inguinale, J. A. M. A. **87**:996 (Sept. 25) 1926.

cases of granuloma inguinale during the past three years and have observed only 2 cases of extragenital involvement. In 1 the involvement was perioral (lips);[18] the other in which the neck was involved, is herein reported. There were pudendal lesions in both cases.

REPORT OF A CASE

A Negress aged 31 was first seen by the police physician at the county jail during the summer of 1935. She had an ulcer of the vulva of two months' duration and received three injections of neoarsphenamine. She was referred to the antisyphilitic clinic of the University Hospital, where she received six more injections of neoarsphenamine. She proved an unreliable patient, returning to

Fig. 1.—Extragenital granuloma inguinale (on the neck) of one year's duration.

the clinic at her whim. During 1936 she received two injections. Early in 1937 she appeared at the antisyphilitic clinic with a 3 by 3 cm. excavated ulcer on the right side of the neck; this was of two weeks' duration. The Wassermann reaction was negative, but the Kahn test was 3 plus. The patient received five intravenous injections of neoarsphenamine and five intramuscular injections of a bismuth preparation; these produced no benefit to the granulomatous ulceration of the neck.

The patient was seen in the granuloma clinic for the first time on Feb. 18, 1938. A 7 by 2 cm. ulceration with clean red raised granulations occupied the

18. Greenblatt, R. B.; Sydenstricker, V. P., and Pund, E. R.: The Fourth and Fifth Venereal Diseases: A Study of One Hundred Consecutive Cases of Granuloma and Lymphogranuloma Inguinale, J. M. A. Georgia **26**:16 (Jan.) 1937.

angle of the neck on the right (fig. 1). Ulcerations similar in appearance to that of the neck occupied the inguinal regions and the greater part of the vulva, which showed elephantiasic enlargement (fig. 2). The lower part of the vagina as well as the cervix was involved in the granulomatous process. She was admitted to the University Hospital for further study on the same day.

A test with bacillary antigen from chancroid and the Frei test gave positive results. The Wassermann and the Kahn reaction were negative. Donovan bodies were readily seen in stained films of material from the pudendal lesions. One cursory examination of stained films of material from the lesion on the neck revealed some suspicious-looking monocytogenic organisms the appearance of which was not conclusive enough for diagnosis. However, histologic study of specimens from both lesions revealed characteristic changes and an abundance of the pathognomonic cells.

Fig. 2.—Granuloma inguinale, showing a striking resemblance between the lesion in figure 1 and the inguinal and vulvar ulcerations.

An initial dose of 1.5 cc. of fuadin was given intramuscularly on Feb. 20, 1938. During the following eight days six injections of 5 cc. of fuadin were given. The patient was then discharged from the hospital and referred to the granuloma clinic for further study. By March 18, 1938, when she had received a total of 51.5 cc. of fuadin, the lesion on the neck was entirely healed. At the time of this report the vulvar, inguinal and cervical granulomatous lesions have healed under continued fuadin therapy.

DIAGNOSIS OF SUSPECTED LESIONS OF GRANULOMA INGUINALE

Of the 9 cases of extragenital lesion culled from the American literature by Fox, in only 2 was the diagnosis confirmed microscopically. Robertson and Sharp[19] were able to demonstrate Donovan bodies in only 20 per cent of a series of cases of granuloma inguinale. Hazen

19. Robertson, J. P., and Sharp, L.: Granuloma Venereum and Lymphopathia Venereum, Am. J. Surg. **34**:322 (Nov.) 1936.

and his associates [20] were able to demonstrate Donovan bodies in 66 per cent of their cases.

Granuloma inguinale should be diagnosed only when Donovan bodies are demonstrated in smears or when biopsy reveals the pathognomonic cell.[21]

The demonstration of Donovan bodies is possible in every case of granuloma inguinale, but may occasionally prove difficult in films from lesions suspected of being granuloma inguinale, for the following reasons:

1. They may be scanty on the surface and may be demonstrable only when smears are taken from a deep part of the lesion.

2. Because of their pleomorphism, they may not be readily recognized. In their atypical immature nonencapsulated forms they may resemble other organisms.

3. The superimposed infection may be so overwhelming as to veil their presence.

These handicaps may be overcome by resort to histologic methods when smears fail to corroborate the clinical diagnosis. Paraffin sections of biopsy material stained with hematoxylin (Delafield's) and eosin or by Dieterle's silver technic [22] will demonstrate the pathognomonic cell and the characteristic inclusion bodies with moderate ease in all cases of granuloma inguinale.

SUMMARY

A case of extragenital granuloma inguinale (neck) in a patient with pudendal lesions is recorded. Examination of stained films from the lesions of the neck was inconclusive, but histologic study revealed the pathognomonic cells and confirmed the clinical diagnosis. The remarkable response of the lesion to fuadin therapy amply demonstrates the specificity of this drug.

---

20. Hazen, H. H.; Howard, W. J.; Freeman, C. W., and Scull, R. H.: Treatment of Granuloma Inguinale in the Negro, J. A. M. A. **99**:1410 (Oct.) 1932.

21. Pund, E. R., and Greenblatt, R. B.: Specific Histology of Granuloma Inguinale, Arch. Path. **23**:224 (Feb.) 1937.

22. Dieterle, R. R.: Method for Demonstration of Spirochaeta Pallida in Single Microscopic Sections, Arch. Neurol. & Psychiat. **18**:23 (July) 1927.

TRICHOSTASIS SPINULOSA

EDWARD F. CORSON, M.D.
PHILADELPHIA

Clumps of hairs which are grossly visible in cases of dermatitis papillaris capillitii are familiar to all dermatologists; they represent the crowding together of more or less adjacent hair follicles by cicatricial masses or active lesions. While the hairs sometimes emerge in tufts from a common aperture, they can be shown to have preserved their individual follicular structures. A less common abnormality is the presence of a quantity of unattached lanugo, in the same follicle. Under the title trichostasis spinulosa Nobl [1] described the latter anomaly in follicular lesions scattered over the thorax and the abdomen. When looking for the condition he found instances rather frequently, 6 cases coming to his attention in a few months. The patients had seborrheic eczema of the scalp and the thorax. A plate accompanying his article was nearly identical with figure 1. The favorite sites in the aforementioned 6 cases were the scapular, the subscapular, the anterior part of the thoracic and the lower part of the abdominal region and the anterior and the posterior aspect of the neck. No mention was made of the conditions occurring on the nose. Galewsky [2] in 1907 reported a case in which the disease occurred on the abdomen. Generalized pyoderma and folliculitis caused the patient to consult the author.

According to Nobl, the anomaly was probably first reported by Franke [3] who called it *"Pinselhaar thysanothrix."* The lesions were follicular and were found on the patient's back in association with comedos. From ten to forty-five fine hairs were removed from each follicle.

The following case would seem to belong in the same category:

REPORT OF A CASE

J. W., a white man aged 46, a contractor, was under observation for seborrheic eczema of the scalp and the face. Examination showed forty or fifty short black plugs projecting from the follicles of the tip and the sides of his nose. They were soft and nonpalpable. The patient had never noticed their appearance. The skin of the nose was practically normal save for follicular pitting and slightly hypertrophic or "bumpy" spots. Thinking that the plugs were broken-off stumps of

1. Nobl, G.: Arch. f. Dermat. u. Syph. **114**:611, 1912-1913; abstracted, J. Cutan. Dis. **31**:588, 1913.
2. Galewsky: Arch. f. Dermat. u. Syph. **106**:215, 1911.
3. Franke, F., cited by Nobl.[1]

hairs (the patient disclaimed having cut any), I removed one with depilatory forceps. It came away painlessly and with slight traction. It was softened with 10 per cent solution of potassium hydroxide and examined under the microscope. A number of filaments were noted, intertwined in a soft, presumably sebaceous stroma. Subsequently twenty or thirty more plugs were lifted out, and some were examined by Dr. Fred D. Weidman. His report follows:

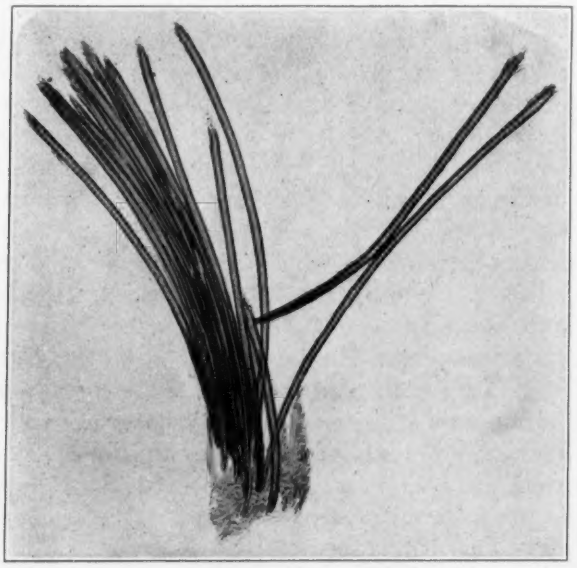


Fig. 1.—Arrangement of a fanlike sheaf of hairs in one follicular plug.

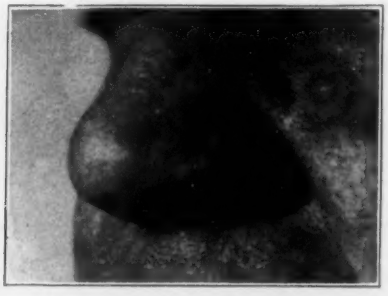


Fig. 2.—Appearance of nose, showing follicular pitting.

"All six specimens were examined microscopically. Two were soaked in undiluted Giemsa solution for several hours or overnight and then quickly differentiated with 95 per cent alcohol and mounted in Farrant solution. Fungi were not found in the material, though the staining was good. However, great masses of extremely small cocci formed a sheath around the entire shaft of the hair and composed a large part of the keratinous plug. Demodex was not observed. In all

specimens the plug consisted of from nine to seventeen delicate lanugo hairs, together with a mass of keratinous material. In one specimen the hairs were almost completely embedded in the latter, while in another the keratinous substance lay closer to the distal than to the proximal extremity of the hair. In all but one of the specimens the periphery of the hair bulb was frayed; in the one specimen the bulb was still well formed and appeared normal but was overlaid by a mosaic arrangement of minute cocci. The hair shafts themselves were well formed, showed no evidence of disintegration and were straight and of uniform diameter. In some of the larger masses the distal ends of the hairs were broken off squarely, whereas in the smaller ones they were normally tapering and rounded.

"A significant observation (at least clinically) was the deep brown discoloration of the distal part of the hair shaft, whether broken off or not. About 50 per cent of the hair shafts concerned were thus affected. At times the color amounted to a deep chestnut brown. It was diffuse, without association of granular pigment.

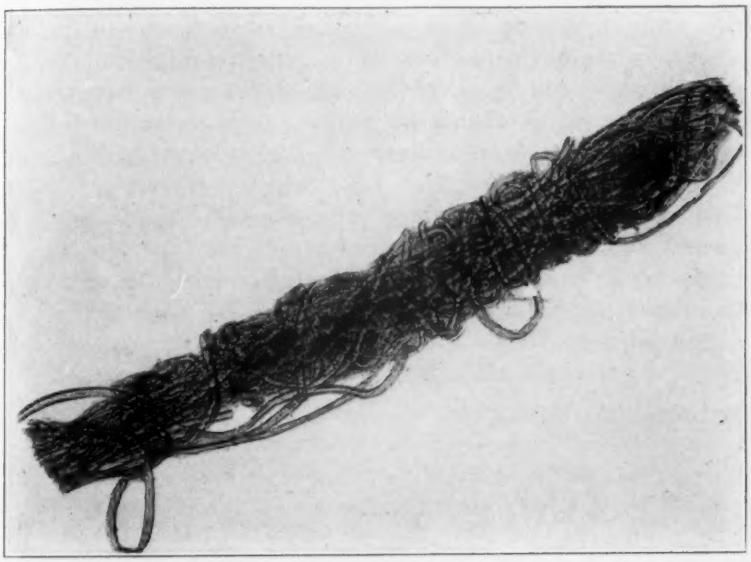


Fig. 3.—Fasces-like arrangement of hairs around a central core of straight and tangled hairs and keratinous material, × 72.

"In only one of the six specimens was there a spirally wound arrangement of hairs. There was a central fasciculus of closely packed hairs, around the entire length of which two or three were spirally wound. In addition, the winding hairs were 'looped' in several places.

"It would appear that the pilosebaceous orifices had become plugged by hyperkeratotic material, as a result of which the successively formed hairs did not dehisce and were retained to such an extent that as many as seventeen specimens accumulated. The brown pigmentation was like the old keratotic material seen in long-standing Darier's disease, ichthyosis and black tongue. It is thus readily understandable why some of the hairs were pigmented and others not; it seems fair to assume that the more recently developed hairs had not yet become pigmented, particularly since specimens containing fewer hairs exhibited less pigmentation."

COMMENT

The patient refused permission for biopsy, and consequently there is available no information as to whether multiple hair papillae were present, whether "bed hairs" contributed to the number of shafts or whether another anomaly existed. An unusually large papilla might conceivably be subdivided into a number of small hair-forming areas, or multiple separate papillae might exist. The shed hairs showed brushy proximal ends and no adherent epithelial sheath. There was a bulb root in one instance. These findings would speak against the presence of multiple papillae. The presence of numerous cocci might explain the successive abortive products of a single papilla without the formation of bedhairs but with abrupt separation of the incomplete shaft. An unusual feature was the occurrence of the condition on the nose, an area not hitherto reported to have been involved. In the plugs one occasionally noted a fasces-like arrangement. While only one of these was mentioned in Dr. Weidman's report, several of that type were observed by me in potassium hydroxide preparations. One was a veritable rope, all the hairs combining in the twist without a central core (fig. 3).

There appears to be no definite embryologic factor responsible for the anomaly, according to the advice of histologists.

Reappearance of the plugs in the affected follicles was rather slow. All available specimens were removed during the patient's first few visits, and after nearly two years the new formations did not protrude sufficiently to permit extraction by forceps.

1201 Medical Arts Building.

DERMATOPHYTOSIS OF THE FEET

SOURCES AND METHODS OF PREVENTION OF REINFECTION

D. A. BERBERIAN, M.D.
BEIRUT, SYRIA

Most of the efforts toward the eradication of dermatophytosis of the feet, commonly known as "athlete's foot," have dealt with the individual patient. Only recently attention has been focused on methods of sterilization of shoes and clothing and on prevention of the spread of infection in such places as shower and locker rooms. Ayres, Anderson and Youngblood [1] recommended fumigation of shoes and clothing with formaldehyde vapor for the control of superficial mycotic infections. Williams [2] drew attention to tinea of the nails as a possible source of reinfection in tinea of the feet. Henderson [3] advised the fumigation of the shoes with formaldehyde as a means of disinfection. Cornbleet [4] stated that the increased amount of sweating associated with diseases of the feet has a tendency to make the ringworm more resistant to treatment. Recently Jamieson and McCrea [5] cultured fifty-three samples of scrapings from shoes of patients suffering from definite fungous infection of the feet and succeeded in isolating known pathogens in sixteen instances. They considered their findings of great significance in revealing the source of recurrences.

I have been studying the possible sources of reinfection for some time, and my findings are significant in explaining the frequency of recurrences. My studies may be divided into the following three groups: (1) investigations designed to ascertain whether stockings and materials used for the lining of shoes may be sources of reinfection—referred to

---

From the Department of Bacteriology and Parasitology, School of Medicine, the American University of Beirut.

1. Ayres, S., Jr.; Anderson, N.P., and Youngblood, E. M.: Fumigation as an Aid in the Control of Superficial Fungus Infections, Arch. Dermat. & Syph. **24**:283-287 (Aug.) 1937.

2. Williams, C. M.: Tinea of the Nails as a Source of Reinfection in Tinea of the Feet: Preliminary Report, Arch. Dermat. & Syph. **18**:730-731 (Nov.) 1928.

3. Henderson, Y.: Fungus Infection of the Feet: Fumigation of Shoes with Formaldehyde as a Means of Treatment, Arch. Dermat. & Syph. **26**:710-711 (Oct.) 1932.

4. Cornbleet, T.: Disorders of the Feet as the Cause of Resistant Eczematoid Ringworm: Their Influence on the Amount of Sweating of the Feet, Arch. Dermat. & Syph. **29**:887-889 (June) 1934.

5. Jamieson, R. C., and McCrea, A.: Shoes: A Source of Reinfection in Ringworm of the Feet, Arch. Dermat. & Syph. **35**:203-210 (Feb.) 1937.

hereafter as endogenous sources of reinfection; (2) experiments with formaldehyde vapor as a disinfectant, and (3) investigations designed to ascertain whether the fungi capable of producing ringworm of the feet can grow on wood, on seaweed and on moist rock covered with débris of moss and other organic matter—referred to hereafter as exogenous sources of reinfection.

INVESTIGATIONS OF ENDOGENOUS SOURCES OF REINFECTION

Stockings of patients suffering from latent, mild or severe infections of ringworm of the feet were obtained; one of each pair was put into a sterile Erlenmeyer flask with about 15 cc. of sterile water; the other stocking was given to the patient to be laundered as usual, with instructions to return it after washing; the washed stocking was then placed

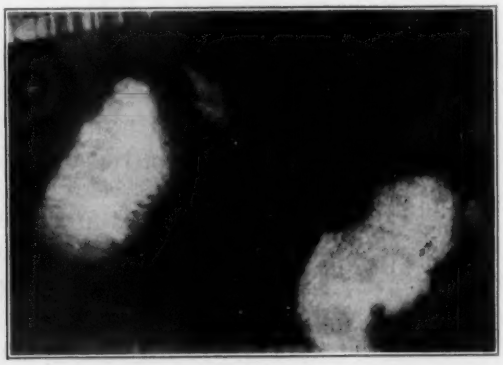


Fig. 1.—Growth of T. interdigitale on stockings obtained from a patient suffering from "athlete's foot."

in a sterile flask with 15 cc. of water and the flask set aside at room temperature. Within three or four weeks typical colonies of Trichophyton interdigitale (Priestley), with which the patients were infected, made their appearance on washed (fig. 1) as well as unwashed stockings. This clearly affirmed two things: (1) that simple laundering does not kill the fungus and therefore that stockings returned from the laundry can still be a source of reinfection; and (2) that the fungus not only remains alive on the stockings but can grow and multiply on them in the presence of sufficient moisture.

I then proceeded to find out whether T. interdigitale could grow equally well on silk, cotton and woolen stockings. Three stockings—one silk, one cotton and one woolen—were put into separate Erlenmeyer flasks with 15 cc. of water and autoclaved. The stockings were then inoculated with spores from a culture of T. interdigitale. Within three

or four weeks there was marked growth on all these stockings, showing that T. interdigitale is capable of growing on the different types of fabric of which stockings are made.

Different types of materials used by shoemakers as inner lining for shoes, including cotton, linen and leather, were inoculated with T. interdigitale in the same way as the stockings. The fungus grew profusely on them (fig. 2), indicating that it could grow and multiply in the shoes of a patient suffering from dermatophytosis.

Fig. 2.—Growth of T. interdigitale, *A*, on material used as inner lining for shoes; *B*, on material used as inner soles for shoes.

EXPERIMENTS WITH FORMALDEHYDE VAPOR AS A DISINFECTANT FOR INFECTED STOCKINGS AND SHOES

The stockings and various lining materials used in the aforementioned experiments and showing growth of T. interdigitale were cut into small squares and put into separate Petri dishes. These dishes, with the tops left open, were then placed on the shelf of a bedside cabinet. Ten or fifteen cubic centimeters of commercial solution of formaldehyde was then put in an open dish and placed in the cabinet, which was closed

tightly. At definite intervals one piece from each Petri dish was removed and put into a tube of Sabouraud's medium. The tubes were incubated at room temperature for ten days and examined for the growth of T. interdigitale. The results of this experiment are recorded in the table.

Stockings and Lining Materials for Shoes Showing Growth of T. Interdigitale Exposed to Formaldehyde Vapor

Material	Length of Exposure					
	2 Hr.	4 Hr.	6 Hr.	12 Hr.	24 Hr.	36 Hr.
Artificial silk stocking	+	+	+	—	—	—
Woolen stocking	+	+	—	—	—	—
Artificial silk stocking, moistened before exposure	—	—	—	—	—	—
Woolen stocking, moistened before exposure	+	—	—	—	—	—
Lining material of shoe	+	—	—	—	—	—
Inner sole of shoe	+	+	—	—	—	—

+ indicates growth of T. interdigitale on Sabouraud's medium; — indicates absence of growth.

The experiment just cited shows that formaldehyde vapor is an effective disinfectant against T. interdigitale and that its disinfecting action is greater and more rapid when the stocking is moistened just before being placed in the disinfecting chamber.

EXOGENOUS SOURCES OF REINFECTION

It is well known that ringworm of the feet is acquired from swimming and bathing grounds, gymnasium floors, etc. Nevertheless, I wanted to determine whether the fungi capable of causing dermatophytosis could grow and multiply in such places. For these experiments cultures of T. interdigitale were used. Sea water, seaweed, bits of wood and pieces of rock covered with moss were brought to the laboratory from the seashore and were placed in Borrel tubes with about 10 cc. of sea water in each. The Borrel tubes were then autoclaved for fifteen minutes at 15 pounds' (6.8 Kg.) pressure. They were inoculated with T. interdigitale and incubated for three weeks at room temperature. The fungus grew well on wood (fig. 3 *A*) and on seaweed (fig. 3 *B*); it grew less luxuriantly on pieces of rock covered with débris of dead moss and dirt.

COMMENT

When one considers that many persons infected with "athlete's foot" walk barefooted on diving boards, on rocks at the seashore and in gymnasiums, disseminating infected epidermal scales containing fungi which are able not only to survive in these places but to grow there, it is easy to understand why "athlete's foot" is becoming so common and

reinfection so frequent. Persons suffering from second, third or fourth degree "athlete's foot" are hardly a menace to others, as they are not able to walk with impunity; patients with latent and mildly active infections are the ones mainly responsible for the dissemination of this infection. The one presumably effective way of protecting oneself against infection or reinfection from these foci of infection is by using rubber slippers.

In view of the experiments just described, the endogenous sources of reinfection, such as one's own stockings and shoes, seem to be much

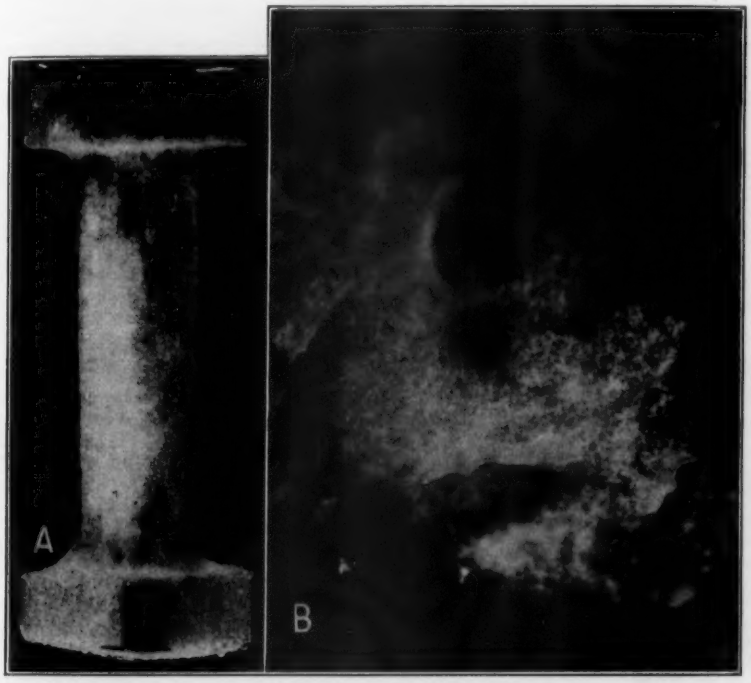


Fig. 3.—Growth of T. interdigitale, *A*, on wood; *B*, on seaweed.

more significant than exogenous sources. Hence, any therapeutic measure directed toward the treatment of the patient's feet alone is bound to meet with disappointment, for after the treatment is stopped the patient is likely to reinfect himself from his own stockings and shoes sooner or later. Therefore, the treating physician should take into consideration the shoes and stockings of the patient.

Sterilization of infected shoes by fumigation with formaldehyde was first recommended by Henderson.[3] This appears to be an effective method of destroying the fungi, as the scrapings from shoes sterilized by this method failed to produce growth when cultured. The steriliza-

tion of stockings is a much more difficult problem. The dermatologist often asks the patient to change his stockings daily and have them boiled, without realizing that woolen and silk stockings may be ruined by boiling.

The simple method of disinfecting shoes and stockings which I have described has proved effective against T. interdigitale, the fungus most commonly encountered in dermatophytosis of the feet. It is therefore recommended that patients suffering from "athlete's foot" place their shoes and stockings in a bedside cabinet or in a special wooden box improvised for this purpose and expose them overnight to the disinfecting action of formaldehyde vapor. Such treatment not only will destroy the fungus but will at the same time preserve the appearance, the color and the fabric of the stockings.

SUMMARY

This study shows that the stockings of patients suffering from athlete's foot are potential sources of reinfection and probably the commonest of those sources. Not only is the fungus found on stockings of patients suffering from the infection, but it survives the ordinary process of laundering and is capable of growing in the fabric.

My experiments prove that T. interdigitale is capable of growth on different kinds of materials used as inner lining for shoes and also on wood, rock, moss and seaweeds. Hence, noninfected persons using the shoes of infected persons or walking on diving boards and on swimming grounds in public baths and gymnasiums are not only walking on infected grounds but actually walking on cultures of fungi capable of causing ringworm of the feet.

A simplified and effective method of sterilizing the infected shoes and stockings of patients suffering from dermatophytosis of the feet is described. The use of all rubber slippers in gymnasiums and on swimming grounds is recommended as a means of safeguarding one's feet against the possibility of infection or reinfection from exogenous sources.

THE SUDORIPAROUS GLANDS

II. THE APOCRINE GLANDS

STUART C. WAY, M.D.
SAN FRANCISCO
AND
ALOIS MEMMESHEIMER, M.D.
ESSEN, GERMANY

As early as 1846, Horner,[1] in describing the odoriferous (apocrine) glands stated:

> I have ventured to give this name to a layer of well marked subcutaneous glands placed in the axilla, and which have been too much neglected by anatomists, indeed there are many modern systems in which they are not even alluded to. They are remarkably well evolved and distinct in the negro, though not peculiar to that race, and are just beneath the skin of the arm pit, embedded in the common adipose cellular membrane and intermixed with the bulbs of the hairs. It is well known in our country that the smell of the negroes is particularly redolent from the axilla: (The same may be said in a qualified way of persons of all complexions); and that some of them, with the strongest efforts to free themselves from it, are so organized that they may be traced by the effluvium with which they impregnate the air.

Shortly afterward, in 1854, von Kölliker,[2] referring to the apocrine glands, said that

> these cell contents, which as I have found, contain much protein and fat, differ considerably from the common sweat, which is fluid and presents no formed elements and probably rather approximates the sebaceous secretion of the skin, on account of which we might be induced to remove these axillary glands from the class of sudoriparous glands and regard their secretion as of a peculiar kind.

Schiefferdecker's [3] investigations in 1922 again brought to our attention the fact that the sudoriparous glands should be divided into the apocrine, or "A," and eccrine, or "E," glands, which may be differentiated by size, development, location and secretory activity.

---

1. Horner, W. E.: Special Anatomy and Histology, ed. 7, Philadelphia, Lea & Blanchard, 1846, vol. 1, p. 378.

2. von Kölliker, A.: Manual of Human Microscopic Anatomy, translated by G. Busk and T. Huxley, Philadelphia, Lippincott, Grambo & Co., 1854, p. 202.

3. Schiefferdecker, P.: Die Hautdrüsen des Menschen und der Säugetiere, ihre biologische und rassenanatomische Bedeutung, sowie die Muscularis sexualis, Stuttgart, E. Schweizerbert, 1922.

Further observations by Pinkus [4] in 1925, Homma [5] in 1926, Herzenberg [6] in 1927, Karrenberg [7] in 1928, Woolard [8] in 1930 and Vohwinkel [9] in 1931 added materially to our knowledge of the subject.

EMBRYOLOGIC AND HISTOLOGIC CHARACTERISTICS

The apocrine gland, together with the sebaceous gland and the hair follicle, develops from the primary germ of the epithelium and is the first form to separate. It is therefore formed from already differentiated epithelium, while the eccrine type develops from undifferentiated epithelium.

After the formation of the gland the distal end of the duct may wander from the hair follicle to empty on the free surface of the skin. The excretory orifice of an eccrine gland, however, never opens into a hair follicle. This peculiarity makes it evident that apocrine glands can be found only where hair exists or has existed.

Apocrine glands differ from other glands of the skin in that they are of a reddish tint instead of yellow and extend more deeply, being found within the subcutaneous tissue.

The cells making up the glands are characterized by their great volume and manner of grouping, being united in groups which give a pitted appearance to cross sections of the axillary skin. Their size renders them easily visible to the naked eye. The glomerulus is 3 or 4 mm. in diameter and formed of a tube, loosely rolled on itself and having alternate regions of narrowing and dilatation. This tube, the diameter of which is from 100 to 200 microns, has a wide lumen lined by a basal layer 2 microns thick and separated from the cells by a layer of epithelial muscle which tends to form a continuous, internal ring that acts as a support to the lining cells. The muscular cells are large and near to one another, while the glandular cells have a somewhat variable shape. At one time they may be polyhedral and vary from 24 to 36 microns in height; at another, cuboidal and from 18 to 24 microns in height. The nuclei of these cells are rounded, and their number varies from one to three. Their location varies, being central when the glands

4. Pinkus, F.: Zur Kenntnis der menschlichen Schweissdrüsen, Dermat. Ztschr. **43**:253, 1925.

5. Homma, H.: On Apocrine Sweat Glands in White and Negro Men and Women, Bull. Johns Hopkins Hosp. **38**:365, 1926.

6. Herzenberg, H.: Neue Beiträge zur Lehre von den apokrinen Schweissdrüsen, Virchows Arch. f. path. Anat. **266**:422, 1927.

7. Karrenberg, C. L.: Histologische Untersuchungen von Achselhöhlenhaut bei beiden Geschlechtern und in verschieden Lebensaltern, Dermat. Wchnschr. **87**:1275, 1928.

8. Woolard, H. H.: The Cutaneous Glands of Man, J. Anat. **64**:415, 1930.

9. Vohwinkel, K. H.: Ueber das Vorkommen von apokrinen Drüsen, Dermat. Ztschr. **60**:314, 1931.

are in the resting stage and toward the base when they are actively secreting. The cytoplasm is filled with granules of yellow pigment as well as others that give a positive reaction to osmic acid and similar stains. The superficial part of the cell is transparent or hyaline and is often so shaped that it projects into the lumen of the gland.

The Act of Secretion.—According to the researches of Brinkmann,[10] the apocrine glands in animals do not function until the maturity of the sex glands. This has been definitely established as true in man.

The eccrine glands produce a fluid which is formed as little droplets within the protoplasm of the epithelial cells of the sweat glands and is then pushed out into the lumen of the gland without any loss of protoplasmic substance.

When secretion occurs in the apocrine type of gland, there appears to be an accumulation of granules near the surface of the cell, and a part of the secreting cell itself is lost during secretion. This takes place in such a way that at first the straight free margin of the epithelial cell is bulged outward toward the lumen of the sweat gland, until a process is formed which becomes narrower and narrower at its base. The cell then ruptures, and the fragmented parts are found within the lumen.

Kölliker [2] stated that it is not improbable that at times the common sudoriparous eccrine glands may be capable of forming and giving forth a cellular secretion similar to that of the apocrine glands.

Chemical Composition of the Apocrine Gland.—Different kinds of granules have been seen in the secreting cells of the apocrine gland. Although osmic acid causes some of these granules to take a light brown stain, it is possible that they may not be fatty, since they fail to react to the ordinary stains for fat and since most body elements can be made to stain in some degree with osmic acid. An intercellular yellowish pigment is present.

About 70 per cent of the specimens showing apocrine glands have shown iron in the epithelium. Homma [8] confirmed the findings of Kölliker,[2] Heynold,[11] Lüneburg [12] and Talke,[13] whose Turnbull blue test showed hematogenous pigments in the axillas.

Klaar [14] stained tissue containing apocrine glands by the berlin blue method of Perls and found hematogenous pigment.

10. Brinkmann, J. H. A.: Die Hautdrüsen der Säugetiere (Bau und Sekretionsverhältnisse), Ergebn. d. Anat. u. Entwcklngsgesch. **20**:1173, 1912.

11. Heynold, H.: Ueber die Knäueldrüsen des Menschen, Virchows Arch. f. path. Anat. **61**:77, 1874.

12. Lüneburg, E.: Beiträge zur Entwicklung und Histologie der Knäueldrüsen in der Achselhöhle des Menschen, Thesis, Rostock, 1902.

13. Talke, L.: Ueber die grossen Drüsen der Achselhöhlenhaut des Menschen, Arch. f. mikr. Anat. **61**:537, 1903.

14. Klaar, J.: Zur Kenntnis des weiblichen Axillaorgans beim Menschen, Wien. klin. Wchnschr. **39**:127, 1926.

Richter [15] not only found iron pigment in the apocrine glands but expressed the belief that these glands lead in secreting cholesterol. Ferruginous granules and cholesterol are present in the apocrine glands from puberty on throughout senility. According to Manca Pastorino,[16] the apocrine glands eliminate, among other things, lipoids and pigment and readily react to acute and chronic diseases such as nephritis and tuberculosis.

Marchionini [17] and, later, Levin and Silvers [18] have shown that considerable difference exists between apocrine and eccrine sweat. Eccrine sweat from the face, the palms, the side of the back and the stomach showed an actual p_H of from 3.8 to 5.6. Apocrine sweat, on the other hand, which was produced in the axilla, showed a p_H varying from 6.2 to 6.9, from which may be drawn the conclusion that the apocrine secretion is less acid and may occasionally become alkaline. In all cases in which readings of the p_H of perspiration from the axillas were compared with those from other portions of the normal skin, Levin and Silvers [18] found an increased p_H. This was regarded as due to the presence of the apocrine glands and to the fact that evaporation of the secretion is delayed because of the opposing cutaneous surface.

Because of this difference in osmotic pressure between apocrine and eccrine sweat, it is believed that the number of dissolved particles is greater in eccrine than in apocrine sweat and that the amount of sodium chloride is less in the apocrine sweat.

Sweat from the apocrine glands, although acid at first, soon becomes alkaline.

In consideration of the facts mentioned, it is interesting to note that certain dermatoses appear in regions where apocrine sweat is present and in intertriginous places where the evaporation of sweat is delayed and the protective acid reactions lost.

DISTRIBUTION OF APOCRINE GLANDS

In order of frequency, the apocrine glands occur in the axillas, the mons veneris, the anus, the abdomen and the breast (about the nipple).

---

15. Richter, W.: Beiträge zur normalen und pathologischen Anatomie der apokrinen Hautdrüsen des Menschen mit besonderer Berücksichtigung des Achselhöhlenorgans, Virchows Arch. f. path. Anat. **287**:277, 1932.

16. Manca Pastorino, V.: Fisiopatologia degli annessi cutanei: Ricerche sulla struttura delle ghiando le apocrine, abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **48**:520, 1934.

17. Marchionini, A.: Physikalisch-chemische Untersuchungen über ekkrinen und apokrinen Schweiss, Schweiz. med. Wchnschr. **58**:1055, 1928.

18. Levin, O. L., and Silvers, S. H.: Possible Explanation for the Localization of Ringworm Infection Between the Toes: Hydrogen Ion Concentration of the Interdigital Spaces of the Feet, Arch. Dermat. & Syph. **26**:466 (Sept.) 1932.

Vohwinkel [9] examined material from many parts of the bodies of twenty Europeans and a larger number of Negroes from San Domingo. In one European only did he discover apocrine glands in a part of the body where they were not described by Schiefferdecker, namely, on the hypogastrium of a middle-aged man. One Negro had them on the forehead and the cheeks.

If, as has been already stated, apocrine glands can occur only on those parts where hair exists or has been, it is reasonable to believe that these glands can occur in uncommon areas in certain persons.

There is reason to believe that apocrine glands occur twice as frequently in women as in men. This was confirmed by Waelsch,[19] who found the large sweat glands of the axillas better developed in women than in men, but this has not as yet been universally accepted.

It seems certain that the apocrine glands are not reduced in old age, in either number or size, although the contrary might be assumed because of their development at puberty.

The work of Fischer [20] has established the Fox-Fordyce disease as one of secretion affecting the apocrine glands. The cystic dilatations of the axillary sweat glands, as described by some authors, represent the normal picture of apocrine glands.

It is interesting that the distribution of Fox-Fordyce disease should have given the clue to its anatomic basis and that the distribution of apocrine glands as given by Schiefferdecker should be so completely confirmed by the locations of this disease.

THE APOCRINE AS ACCESSORY SEXUAL GLANDS

Rebaudi [21] has called attention to the enlargement of the apocrine glands in pregnant women and especially in those with eclampsia. Loeschcke [22] noticed the participation of apocrine glands in the sexual cycle of women—that is, they enlarge and secrete more actively at the time of menstruation. Later Waelsch,[19] Kayser [23] and Seitz [24] confirmed

19. Waelsch, L.: Ueber Veränderungen der Achselschweissdrüsen während der Gravidität, Arch. f. Dermat. u. Syph. **114**:139, 1912.

20. Fischer, H.: Fox-Fordyce Disease: Preliminary Report, Dermat. Wchnschr. **80**:821, 1925.

21. Rebaudi, S.: Der Schweissdrüsen-Apparat während der normalen und der pathologischen Schwangerschaft, Beitr. z. Geburtsh. u. Gynäk. **17**:11, 1911.

22. Loeschcke, H.: Ueber zyklische Vorgänge in den Drüsen des Achselhöhlenorgans und ihre Abhängigkeit vom Sexualzyklus des Weibes, Virchows Arch. f. path. Anat. **255**:283, 1925.

23. Kayser, F.: Achselhöhlenbrüste bei Wöchnerinnen, Arch. f. Gynäk. **85**:459, 1908.

24. Seitz, L.: Ueber eine mit Schwellung einhergehende Hypersekretion der Schweiss- und Talgdrüsen in der Achselhöhle während des Wochenbettes, echte Milchsekretion vortäuschend, Arch. f. Gynäk. **80**:517, 1906.

this observation. Others have expressed the belief that these glands function from the beginning of sexual maturity independently of the sexual cycle throughout the life of the person. The studies of Herzenberg [6] compelled her to the belief that the apocrine glands are influenced by physiologic rather than pathologic sexual occurrences.

TABLE 1.—*Apocrine and Eccrine Glands Compared Anatomically and Otherwise*

	Eccrine Glands	Apocrine Glands
Origin of glands	Undifferentiated epithelium	Differentiated epithelium
Time of development	Before birth	At puberty
Number present	Many	Few
Location	Generalized, except anterior surfaces of nails, labia minora, inferior parts of labia majora, inner surface of prepuce, glans and internal part of pinna of ear	Axilla, anus, mons veneris, breast and abdomen
Size of ducts	Small	Large
Secretion	More fluid	Less fluid
Glands give forth a secretion without loss of substance from secreting cells	Yes	No
Glands stain deeply with hematoxylin	Yes	No
Stronger, muscular layer surrounding the epithelial cells	No	Yes
Presence of iron in secreting cells	No	Yes
Glands are more coiled and narrower at distal end	Yes	No
Gland is usually connected with hair follicle	No	Yes
Glands always open directly on surface of skin	Yes	No
Size of gland	Small	Large
Chemical reaction of sweat	p_H 3.8-5.6	p_H 6.2-6.9

TABLE 2.—*Results of Study of Tissue*

Cause of Death	No. of Cases	Secretory Activity (Percentage)	Percentage in Which Hemosiderin Was Present	Percentage in Which Hemofuscin Was Present	Percentage in Which Cholesterol Was Present
Cancer	9	78	78	67	89
Pneumonia	7	57	42	29	57
Tuberculosis	4	100	100	100	75
Miscellaneous	12	75	50	56	75

The supposition is that apocrine glands are functional in women from the beginning of sexual maturity until old age. During the intermenstrual period and after the climacteric their function manifests itself within moderately narrow limits. During the premenstrual period and during pregnancy there are hypertrophy and hypersecretion of the

Fig. 1.—Postmortem section of axillary tissue from a patient who died of emphysema, stained with hematoxylin and eosin, showing actively secreting apocrine glands (× 600).

Fig. 2.—Postmortem section of axillary tissue from a patient who died of lobar pneumonia, stained with hematoxylin and eosin, showing apocrine glands that have recently secreted (× 400).

Fig. 3.—Postmortem section of axillary tissue from a patient who died of syphilis and arteriosclerosis, stained for iron reaction with ammonium sulfide (Mallory), showing black granulates of hemosiderin in an actively secreting apocrine gland (× 600).

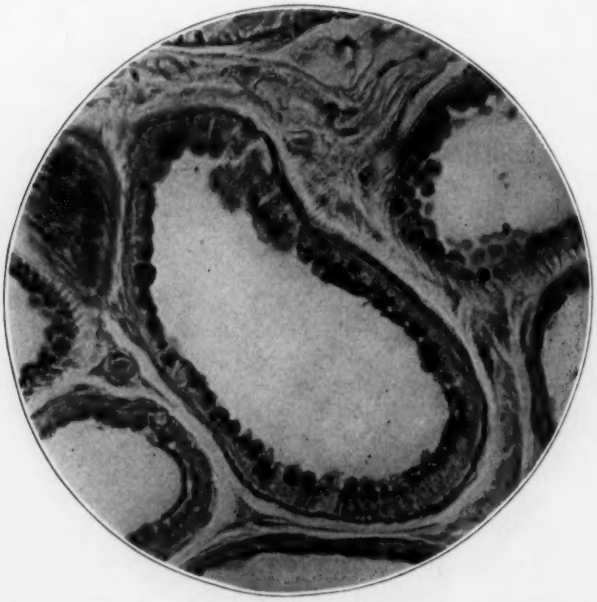


Fig. 4.—Postmortem section of axillary tissue from a patient who died of lobar pneumonia, stained for iron reaction with ferrocyanide of potassium (Mallory), showing granules of hemofuscin and hemosiderin in an apocrine gland during an early secretory stage (× 400).

glands. These findings show an obvious correlation between the apocrine glands and the sexual organs and justify the name "accessory sexual glands."

Tewfik [25] likewise has expressed the belief that the apocrine glands are directly related to the genital tract through their physiologic activity, in that they play an important role during excitement, fertilization and nursing and in the presence of certain diseases of the skin.

Fischer,[26] by questioning his female patients, learned that just before menstruation the axillary changes were similar to and simultaneous with the swelling and hardening of the mammae.

Brinkmann [10] has expressed the belief that the odor of the secretion of the apocrine glands increases sexual excitement while others have stated that it is responsible for the characteristic body odor of a person and an accurate index of his health. Body odor has been known to be identical in male members of several generations of a family.

MICROSCOPIC STUDY

Axillary material removed post mortem from 32 subjects was carefully studied. Special attention was given not only to the size and the number of glands present but to the presence or absence of iron and cholesterol within the cells.

In order to overcome errors in staining, three or more sections from each subject were stained by the same method. In those cases in which there was a negative reaction to Mallory's potassium ferrocyanide, the reaction for iron with ammonium sulfide was used as a control.

SUMMARY

Apocrine glands occurred with the same frequency and seemed equally well developed in male and female subjects.

One man and one woman retained the eccrine type of gland. This failure to develop at puberty could not be explained.

The axillary glands in 89 per cent of the 27 adult subjects were either actively secreting at the time of death or had recently secreted.

The glands in 78 per cent of adults gave positive reactions of varying degrees to Mallory's potassium ferrocyanide and ammonium sulfide stains.

The low percentages obtained in table 2 for patients who died of pneumonia were due to the number of infants in this classification.

25. Tewfik, H.: Die apokrinen Drüsen der Achselhöhle, abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **43**:619, 1932.

26. Fischer, H.: Zur Fox-Fordyceschen Krankheit, Arch. f. Dermat. u. Syph. **156**:583, 1928.

Axillary tissue from five subjects varying in age from 8 to 18 months showed the eccrine type of gland and a complete absence of iron (hemosiderin and hemofuscin).

From such a small series of cases it is impossible to draw definite conclusions. There seems, however, to be a definite relation between cellular activity and the amounts of hemosiderin, of hemofuscin and of cholesterol present.

Apocrine glands deserve to be classified as "accessory sexual glands."

MOUSE BRAIN LYMPHOGRANULOMA VENEREUM ANTIGEN

CLINICAL EXPERIENCE AT CLEVELAND CITY HOSPITAL

GEORGE W. BINKLEY, M.D.
AND
WILLIAM R. LOVE, M.D.
WITH THE COLLABORATION OF
WALTER F. SCHWARTZ, M.D.; JOSEPH M. HITCH JR., M.D.,
AND GRACE A. MARGARD, A.B.
CLEVELAND

For the past six years lymphogranuloma venereum antigen has been prepared at the Cleveland City Hospital according to the method of Frei.[1] The specificity of this antigen is attested by cases reported from this hospital by DeWolf and Van Cleve,[2] Cole [3] and Connor, Levin and Ecker [4] and from other clinics by de Gregorio [5] and Flandin and Turiaf.[6]

Recently there has been an opportunity to test some commercial Frei antigen [7] made from "a saline suspension of killed lymphogranuloma virus in mouse brain." This antigen was used concomitantly with our own antigen and with an emulsion of normal mouse brain as a control. We have never used it alone for the diagnosis of lymphogranuloma venereum in new cases.

From the Department of Dermatology and Syphilology, Service of Drs. H. N. Cole and J. R. Driver, Cleveland City Hospital and Western Reserve University, School of Medicine.

1. Frei, W.: A New Skin Reaction in Lymphogranulomatosis Inguinalis, Klin. Wchnschr. **4**:2148 (Nov. 5) 1925.

2. DeWolf, H. F., and Van Cleve, J. V.: Lymphogranuloma Inguinale, J. A. M. A. **99**:1065 (Sept. 24) 1932.

3. Cole, H. N.: Lymphogranuloma Inguinale, Fourth Venereal Disease: Its Relation to Stricture of the Rectum, J. A. M. A. **101**:1069 (Sept. 30) 1933.

4. Connor, W. H.; Levin, E. A., and Ecker, E. E.: Observations on the Frei Test, J. Infect. Dis. **60**:62 (Jan.-Feb.) 1937.

5. de Gregorio, E.: Study of Allergy in Subacute Lymphogranuloma Inguinale, Ann. d. mal. ven. **30**:727 (Oct.) 1935.

6. Flandin, C., and Turiaf, J.: Technic and Value of the Frei Reaction in Nicholas-Favre's Disease, Bull. Soc. franç. de dermat. et syph. **43**:320 (Feb.) 1936.

7. This antigen was furnished by Arthur F. Coca, of Lederle Laboratories, Inc., Pearl River, N. Y.

Our experience with commercial Frei antigen prepared from mouse brain according to the method of Grace and Suskind [8] has been such that we are loath to have such an antigen supplant the original human Frei antigen. Moreover, the objections to the human antigen which were raised by Grace and Suskind have not been found valid in this clinic. There has never been a lack of human antigen. Cases of suppurating bubo due to the virus of lymphogranuloma venereum have been encountered sufficiently often to enable us to prepare and supply Frei antigen to all dermatologists in Cleveland and to respond to calls from many dermatologists in other parts of the continent. Patients with uncomplicated lymphogranuloma venereum (bubo) suitable for antigenic purposes have yielded adequate pus. Since Frei antigen is correctly made by diluting pus with 4 parts of physiologic solution of sodium chloride and an average bubo yields 10 cc. of pus, 50 cc. of finished antigen can be prepared, which will provide material for 500 intradermal tests. In answer to the problem of varying antigenic contents, it is obvious that with the supply of potent antigen always more than adequate, we never hesitate to discard weak human Frei antigen.

REVIEW OF LITERATURE

Other investigators have had difficulty with Frei antigen prepared from infected nerve tissue. Frei antigen prepared from the nervous system of monkeys was found unreliable by Levaditi, Durel and Reinié.[9] They concluded that the amount of virus contained in the brains of infected monkeys may vary considerably, even under the same experimental conditions; that the only reliable antigen for use in the diagnosis of lymphogranuloma venereum is human antigen, and that only antigens that have been proved reliable should be used.

De Blasio [10] investigated the specificity of antigen prepared from monkey brain, supplied by the Pasteur Institute, and concluded that the value of that antigen has been greatly exaggerated and that it is by no means specific.

---

8. Grace, A. W., and Suskind, F. H.: (*a*) Lymphogranuloma Inguinale: II. The Cultivation of the Virus in Mice and Its Use in the Preparation of Frei Antigen, Arch. Dermat. & Syph. **33**:853 (May) 1936; (*b*) Lymphogranuloma Inguinale: III. The Use of Lymphogranulomatous Mouse Brains for Diagnosis, ibid. **34**:65 (July) 1936; (*c*) Use of Standardized Mouse Brain Antigen for Performance of Frei Test for Lymphogranuloma Inguinale, J. A. M. A. **107**:1359 (Oct. 24) 1936.

9. Levaditi, C.; Durel, P., and Reinié, L.: Diagnostic Value of Frei's Antigen from Monkeys, Bull. Soc. franç. de dermat. et syph. **42**:1639 (Nov.) 1935.

10. De Blasio, R.: Non-Specificity of the (Monkey Brain) Frei Reaction, Bull. Soc. franç. de dermat. et syph. **43**:344 (Feb.) 1936.

Flandin and Turiaf [6] compared the antigen prepared from monkey brain with that from human pus. They stated: "Monkey antigens vary spontaneously with time and have to be standardized (or evaluated) at each reading with a good human antigen." On the basis of their results in 400 cases they stated that it is more desirable to use a good human antigen which is specific and stressed the necessity of reading the result on the fourth day after injection.

Strauss and Howard,[11] using commercial Frei antigen made from mouse brain and their own preparation from mouse brain, concluded that "sensitivity to mouse brain is common enough to lead to a large number of false positive reactions if mouse brain antigens are used for the diagnosis of lymphogranuloma inguinale," and that "the false reaction is induced in normal subjects as well as in patients with lymphogranuloma inguinale."

Von Haam and Hartwell [12] found that neither the specificity nor the sensitivity of Frei antigen made from mouse brain is altered by preservation in the ice box or at room temperature for as long as fourteen months.

However, it is recognized that to make the intradermal test for lymphogranuloma venereum available to physicians generally a standard, specific commercial antigen would be desirable. Therefore, we undertook the clinical evaluation of mouse brain antigen with real enthusiasm.

METHOD

A series of intradermal injections was made on the flexor surface of the right forearm (the left forearm is reserved for intradermal injection of Haemophilus Ducrey vaccine), the most proximal injection being made with human Frei antigen; the middle one with commercial Frei antigen, made from mouse brain and the distal injection with a commercial emulsion of normal mouse brain.

With separate "allergy" needles (*27* gage, 3/8 inch [0.95 cm.] long), 0.1 cc. of each antigen was used for the injection. The reactions were read in forty-eight, seventy-two and ninety-six hours. The cutaneous reactions to Frei antigen have always been recorded in this clinic by the use of minus and graduated plus signs. The tabulation shows the approximate size of the papules designated by the various signs. With this scale as a guide, the cutaneous reactions were noted in the "Frei book" by two observers.

Sign	Approximate Size of Papule, Mm.
—	2-3
+	3-4
++	4-6
+++	6-8
++++	8-10 and larger

11. Strauss, M. J., and Howard, M. E.: Frei Test for Lymphogranuloma Inguinale: Experiences with Antigens Made from Mouse Brain, J. A. M. A. **106:** 517 (Feb. 15) 1936.

12. von Haam, E., and Hartwell, R.: Value of Mouse Brain Antigen for Diagnosis of Lymphogranuloma Inguinale, Proc. Soc. Exper. Biol. & Med. **36:**269 (April) 1937.

RESULTS

The results of the intradermal tests in a series of 88 subjects without lymphogranuloma are recorded in table 1. In this control group, the tabulators have recorded no false positive reactions to human Frei antigen, i.e., no reactions larger than 6 or 7 mm. were found. In the same subjects the mouse brain antigen produced a number of +++ and ++++ reactions, of which an average of 45 per cent were recorded as false positive after ninety-six hours of observation.

Further analysis shows an average of 32.5 per cent +++ and ++++ reactions to the control emulsion of normal mouse brain. In figure 1 *A* is shown one of the reactors to emulsion of normal mouse

TABLE 1.—*Positive Reactions Among Subjects without Lymphogranuloma Venereum*

Substance Used in Test	71 Males			17 Females		
	48 Hours	72 Hours	96 Hours	48 Hours	72 Hours	96 Hours
Human antigen	0	0	0	0	0	0
Mouse brain antigen	53 (74.5%)	46 (65.5%)	34 (48%)	11 (65%)	12 (71%)	7 (41.2%)
Emulsion of normal mouse brain	45 (63.2%)	35 (49.5%)	21 (30%)	11 (65%)	10 (58.8%)	6 (35%)

TABLE 2.—*Positive Reactions Among 37 Patients with Lymphogranuloma Venereum, of Whom 6 Were Women*

Substance Used in Test	48 Hours	72 Hours	96 Hours
Human antigen	37 (100%)	37 (100%)	37 (100%)
Mouse brain antigen	37 (100%)	37 (100%)	37 (100%)
Emulsion of normal mouse brain	11 (30%)	12 (32.5%)	12 (32.5%)

brain and to mouse brain antigen. There was no reaction to human Frei antigen (ringed area).

The reactions to the same three antigens in 37 cases of known lymphogranuloma venereum are recorded in table 2.

The reactions in this group confirm the previous reports of the specificity of the original Frei antigen. Likewise, the emulsion of mouse brain infected with the virus of lymphogranuloma venereum produced strongly positive reactions in all subjects known to have or to have had lymphogranuloma venereum. As in the control group of patients without lymphogranuloma, however, there was a high percentage of cases in which the emulsion of normal mouse brain produced a reaction. In figure 1 *B* is shown a type of reaction commonly obtained in cases of proved lymphogranuloma venereum. In figure 2

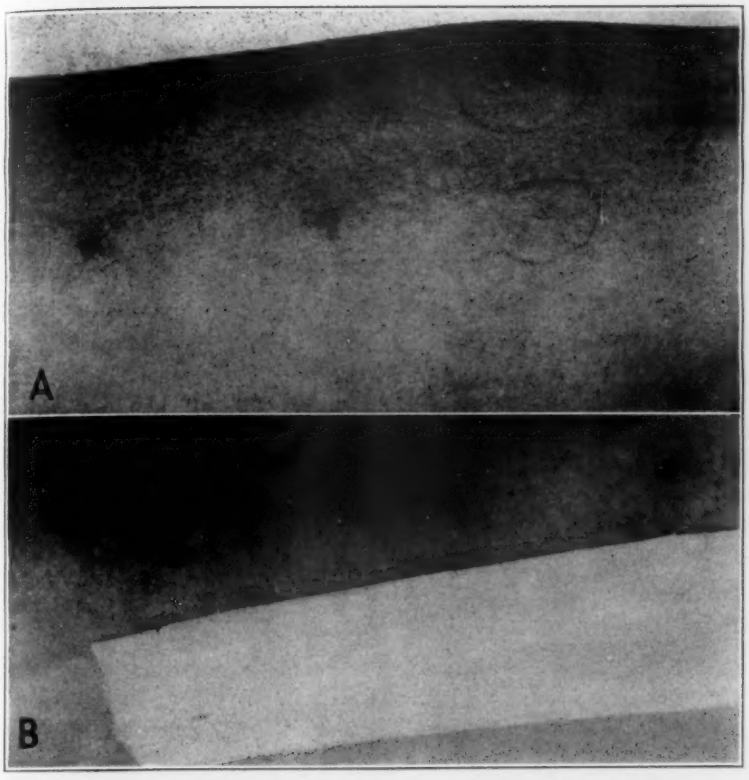


Fig. 1.—*A*, the ring surrounds the site of an injection of Frei antigen. The reaction to the mouse brain antigen is distal to it, and more distal is the reaction to emulsion of normal mouse brain. *B* shows positive reactions to both human and mouse brain antigen, but the reaction to the control test is positive (0.5 cm.).

Fig. 2.—Human and mouse brain antigen produce equally positive reactions in a case of lymphogranuloma venereum, while the reaction to the control test (ringed area) is negative.

are the reactions which were obtained in a person with active lymphogranuloma venereum who was not sensitive to emulsion of normal mouse brain. The control injection caused no reaction.

SUMMARY

In this clinic it was found that 1 of every 3 subjects with or without lymphogranuloma venereum had a positive reaction to intradermal injection of control normal mouse brain. An even more serious defect in the test was the 45 per cent of false positive reactions to Frei antigen prepared from mouse brain in cases in which a good human Frei antigen gave negative results. This may be due in part to human sensitivity to normal mouse brain, as indicated by the 33 per cent of reactions to the emulsion of normal mouse brain. This number of false positive reactions indicates that mouse brain is as impracticable a medium for the virus as monkey brain has been found to be.

We are in full accord with Strauss and Howard in their opinion that

> the size of a papule does not lend itself to exact measurement and for this reason it is quite conceivable that a papule 5 or even 4 mm. in diameter might frequently be read as a positive test.

Moreover, any cutaneous test which does not produce clearcut positive reactions, as compared with definitely negative reactions to control tests, but instead depends on the mathematical result obtained by subtracting the size of a control dermal papule from the size of a diagnostic dermal papule has a handicap which no other diagnostic intradermal test possesses.

CONCLUSIONS

1. Frei antigen prepared from mouse brain produces positive dermal reactions in subjects who have been infected with lymphogranuloma venereum, but it frequently produces the same dermal reaction in other subjects.

2. Emulsion of control normal mouse brain causes doubtful to positive reactions in both groups of subjects.

3. For these reasons the Western Reserve Clinic continues to use human Frei antigen and deems that Frei antigen prepared from mouse brain is not suitable for the diagnosis of lymphogranuloma venereum.

10515 Carnegie Avenue.

DERMATOLOGIC SYMPTOMS OF VITAMIN DEFICIENCIES

HERMAN GOODMAN, M.D.
NEW YORK

The clinical problems of deficiency of vitamins presented by cutaneous lesions have been recognized within the past decade. The pioneers of dermatology recognized a relation between dietary metabolism and the skin but did not know about vitamins. The literature on the influence of vitamins on the skin pertinent to the present review is recent. No published record in English is complete.

Mouriquand and Gaté gave an ambitious outline before the Ninth International Congress of Dermatology and Syphilology at Budapest, Hungary, Sept. 13 to 21, 1935. They separated the clinical and experimental features under each of the initialed vitamins. Much space was given to pellagra. No bibliography was included in their report, and many statements were credited to oral communications.

Pasini, of Milan, Italy, discussed the paper of Mouriquand and Gaté. These authors, he said, had made a general pathologic exposition of the cutaneous reactions due to a lack of vitamins. He called on clinical dermatologists to give a classification adapted to avitaminosis. The questions had not been sufficiently studied to allow presentation of a complete and definite grouping. Comel, of Pasini's clinic, made his research under the general title of dysvitaminoses cutanées. There were three divisions:

1. The true dysvitaminoses, i. e., dermatoses with a mechanism and pathogenesis essentially a part of the vitamin disease, such as scurvy and possibly pellagra.

2. The relative dysvitaminoses, i. e., dermatoses accompanying definite vitamin disease, but of which the exact factor of the vitamin responsible is not known, such as papulofollicular syndromes of avitaminoses A and B and the cutaneous dystrophies.

3. Paravitaminoses, i. e., classic dermatologic concepts of which a lack of vitamins is only a secondary cause, although the cutaneous pathologic processes are distinct. Eczema (certain types) and psoriasis may be interrelated with the dysvitaminoses, in that the latter may have some share in the pathogenesis of the cutaneous disease.

All the available references to lack of vitamins and its effect on the skin have been abstracted or noted in the following paragraphs:

VITAMIN A

Bloch stressed the relation of vitamin A to xerophthalmia. He described the dry and shriveled scaly skin of infants affected.

Pillat observed avitaminosis A among 3,000 soldiers near Peiping, China. The cutaneous eruption preceded the ocular changes.

Frazier and Hu reported extensively on the peculiar papular cutaneous eruption of persons with avitaminosis A. There were 207 patients from 2 months to 57 years of age. A follicular eruption was characteristic of the disease among those who had reached sexual maturity and was not observed in children. Simple xerosis in infants or preceding follicular keratosis in adults was due to avitaminosis A. Abeyance of function of the glands of secretion of the skin was a conspicuous sign. Frazier and Hu noted that pyogenic dermatoses occurred frequently as a late manifestation. Comedos of the face were associated abnormalities. They were more keratotic than the comedos of acne, and pustules were rare. The acne-like eruption was present in groups aged over 18 years. In 11 per cent of these, the comedo was the only cutaneous abnormality other than the general xerosis.

Various other changes in the skin have been advanced as caused by lack of vitamin A. These include infantile seborrheic eczema, hyperkeratosis, psoriasis and redness of the skin of infants. Kuipers reported good results in cases of infantile seborrhea from doses of vitamin A combined with hydrochloric acid. Urbach in 1932 stated that he awaited confirmation of the observation.

Loewenthal observed 130 cases of dermatitis due to avitaminosis A among prisoners in Africa. In addition to xerophthalmia, keratomalacia and night blindness, he listed dryness, harshness and irritation of the skin. Increased keratinization of the skin and a papular acneform eruption with comedo formation were reported, as well as lack of luster and brittleness of nails. Treatment with cod liver oil led to improvement of ocular symptoms in 100 per cent and of cutaneous eruptions in 98 per cent of cases.

Nicholls proposed the name phrynoderma for the disease he described as a papular dry eruption of the skin frequently accompanied with a mild neuritis and/or ocular symptoms of night blindness, dimness of sight, xerophthalmia and keratomalacia. The patients were subject to diarrhea or dysentery. When this occurred, the neuritis became marked and the mortality was high. The disease was due to vitamin A deficiency, but other food factors may have been involved. In a later paper Nicholls associated sore mouth with phrynoderma. He grouped xeroderma (Malcolm Morris), keratosis pilaris, pityriasis pilaris and keratosis suprafollicularis as similar to phrynoderma. The natives of Ceylon were commonly afflicted with the cutaneous symptoms and keratomalacia. Their diet contained a minimum of fat-soluble vitamin.

Lauber reported that vitamin A definitely aided healing of surgical wounds and was valuable in cases of acute infection.

Mackay found that babies fed solely on milk and table food without extra vitamin A were more susceptible to diaper dermatitis, intertrigo and dribbling dermatitis than those babies who received extra vitamin A. A slight deficiency of vitamin A diminished the resistance of the skin to infection.

Scheer and Keil reported 2 cases of vitamin A deficiency coexisting with scurvy. The cutaneous lesions of avitaminosis A were not distinguishable from those of mild scurvy.

Goodwin reported a case in which dry, harsh "goose skin" with a marked papular eruption on the extensor surfaces was ascribed to lack of vitamin A. Loewenthal saw the patient and found features similar to those in the group of cases he had reported from Africa. The condition was due to a deficiency of vitamin A in the diet and was completely cured by a good mixed diet plus cod liver oil. Mackay, in a comment at the close of Goodwin's article, wrote that she was convinced that one cutaneous symptom was sufficient for diagnosis of vitamin A deficiency and that the therapeutic test was the most valuable indication of the condition.

Sweet and K'Ang had 203 Chinese patients with vitamin A deficiency. Cutaneous, capillary and ungual symptoms were similar to those previously described. All the lesions improved when specifically treated by administration of vitamin A.

Redaelli reported that infants with weeping eczema showed improvement during administration of vitamin A.

Palloti studied rats that had been kept on a diet lacking vitamin A for nine months. He observed loss of hair, erythema and desquamation. Histologic studies showed hyperkeratosis and atrophy of the hair follicles and the sebaceous glands. There was formation of spindle-shaped cells in nests similar to that in cancroid. Dyskeratosis has frequently been reported as part of avitaminosis A.

Pettler noted improvement of clinical pityriasis rubra pilaris during administration of vitamin A. He commented on the clinical and histologic similarities between its cutaneous manifestations and avitaminosis A.

Busman and Hegarty presented a man suspected of vitamin A deficiency who showed a generalized follicular papular eruption which was pruritic and distinctly grater-like.

Müller administered vitamin A therapeutically. He tried out commercial products in a case of Wilson-Brocq dermatitis exfoliativa generalisata.

Reiss stressed hypovitaminosis rather than avitaminosis in his review of deficiency of vitamin A. He drew attention to the changes in the nails and to perlèche-like conditions.

Munella studied the influence of vitamin A on the growth of hair of rats.

Giblin reported an eruption similar to that recorded by Loewenthal among Papuan natives.

Radhakrishna Rao described the histologic changes associated with vitamin A deficiency, cutaneous lesions as superficial noninflammatory hyperkeratosis of the epithelium of the epidermis and hair follicles, distention of the orifices of pilosebaceous follicles by horny plugs and atrophy of the sebaceous glands with impaired function of the sweat glands.

Jeghers summarized clinical data on 50 persons with subnormal dark adaptation and found 15 to have dryness of the skin, 2 hyperkeratosis, 3 itching and 2 acne. Among 50 persons with normal dark adaptation, he found 2 with dryness of the skin, 2 with acne and none with either hyperkeratosis or itching.

Sternberg and Pillsbury concluded that avitaminosis A in rats had no apparent effect on the resistance of the skin to experimentally produced infection with streptococci and staphylococci.

Excess vitamin A has been reported as fatal to rats. Lipoid accumulates in the endothelium and the epithelium. The coat becomes shaggy, and the hair of the snout falls.

Jacobs reported a papular eruption in infants as a manifestation of hypervitaminosis A.

Comment.—Improvement has been noted in keratinized pilosebaceous apertures of the upper arms and the thighs of young girls when they were placed on balanced diets and given butter. Similar excellent results have followed the administration of 1 grain (0.06 Gm.) of whole pituitary gland by mouth daily. The question is propounded: Will a relation be established between the pituitary hormones and vitamin A?

VITAMIN B_1

It is difficult to evaluate the cutaneous lesions caused by lack of vitamin B_1. The lesions depend on the general bodily symptoms rather than specifically on avitaminosis B_1. Cutaneous lesions follow the clinical course of polyneuritis in the dry form and of edema in the wet form.

Sharples noted a burning sensation of the soles so intense as to prevent the patient's working for weeks at a time as due to lack of vitamin B_1 in adult beriberi. Bacterial infection was uncommon. Cure was effected by administering generous portions of properly cooked rice, eggs, fowl or beef soup, fresh fruit and vegetables and milk. Vitamins were not mentioned in the report.

Gerstenberger used water-soluble vitamin B in canned tomato juice with success in treating herpes labialis, herpetic stomatitis and other diseases of the mucous membrane.

Redaelli treated 33 children with vitamin B and a low fat diet. These showed favorable responses.

Comment.—Acrodynia has the name dermatopolyneuritis among others. It signified to Thursfield and Paterson in 1922 a concept not unlike that of avitaminosis B_1. Von Westreman, Debré and Petot reported 3 cases from Rotterdam, Netherlands. They upheld the theory that the disease was caused by deficiency in diet, avitaminosis and secondary infection. They secured good, although delayed, results from administration of a balanced diet high in vitamins. McClendon successfully treated patients with this disease by adding yeast and viosterol to the diet. Pearlman reported complete recovery of a patient with acrodynia when a diet high in vitamins was given without other treatment. Zahorsky found treatment of a 9 month old infant with ultraviolet rays from a quartz lamp and tonics ineffective; addition of yeast to the diet caused improvement. Miss Burr and I reported several cases fully several years ago and gave a bibliography.

VITAMIN B_2(G)

The nomenclature of B_1 and B_2 is misleading, as neither chemically nor physiologically are the two vitamins similar.

Guha advanced the idea that pellagra was a complex syndrome arising from an association of various factors, in which the deficiency of an antipellagra factor—possibly but not necessarily identical with the growth-promoting vitamin B_2—is the main but not the sole factor. The cutaneous lesions of pellagra include redness of the backs of the hands and the neck, of the wrists, of the scrotum and of the feet. Added pigment is part of the picture. The factor of sunlight seems important, but lack of vitamin B_2(G) and certain dietary deficiencies must be present in addition.

Deficiency of vitamin B_2 (G) favors loss of hair in experimental animals.

Gurin and Eddy expressed doubt whether the dermatitis of rats resulting from a diet was due to the absence of a factor identical with that which prevents pellagra in human beings.

Sweitzer expressed the belief that so-called alcoholic pellagra and true pellagra are identical and are due to the lack of the same vitamins, particularly B_2(G).

Hogan and Richardson found that vitamin B is really a mixture of at least two vitamins. Vitamin B_1 prevents polyneuritis, and vitamin B_2(G) prevents dermatitis. Irradiation destroys the antidermatitis factor. In rats receiving irradiated yeast as the sole source of vitamin

B_2(G) characteristic dermatitis developed, with 100 per cent mortality. The external lesions were limited to the feet, the muzzle, the eyes and the ears. No loss of fur except in the affected area was noted. The dermatitis developed in an average of thirty-four days in a series of 43 animals fed a diet free from vitamin B_2(G) after weaning. The average period of survival was fifty-one days after weaning.

Dann was satisfied that rat dermatitis due to deficiency in vitamin B_6 was not analogous to the dermatitis of human pellagra. Exposure to light was not a necessary factor in the production of rat dermatitis.

Copping maintained young rats on diets lacking only one of the constituents of vitamin B_2. Those deprived of riboflavin manifested a cutaneous disease in which the hair is shed without swelling or inflammation; bald patches develop, especially over the head and the face, and the eyelids are often stuck together with a serous blood-stained fluid which exudes from the eyes and from the nostrils. In those deprived of vitamin B_6 a symmetric florid dermatitis characterized by redness, swelling and edema appeared, affecting first the paws and the tips of the ears and the nose. In 5 rats out of 10 of the former group cure was observed and growth restored by the administration of pure ribroflavin. In the latter group, speedy and complete cure was obtained by the administration of vitamin B_6 in an alcoholic extract of whole maize or wheat; cure was more irregular and imperfect when vitamin B_6 was given in the form of a preparation of yeast.

Comment.—In Virginia twenty-five years ago I had the opportunity of observing cases of pellagra. In one family the head of the house was married for the third time. His 2 previous wives had had pellagra, and one had died with typical cutaneous and nervous symptoms. In the third wife, more youthful than the others, pellagra developed the summer I lived with the family. The husband, 2 grown children by former marriages, 1 infant by the third wife, the patient and I partook of the same food. Except for "fat back," the diet was about the same as I had eaten at northern farmhouses during previous summers.

About 1922, with Dr. M. Parounagian, I observed cases of alcoholic pellagra or pseudopellagra among homeless drinkers of "smoke," or prepared alcohol intended for combustion. True pellagra and pseudopellagra are indistinguishable clinically in my opinion.

VITAMIN C

Smith (quoting Sherman and Smith) noted that a hemorrhagic disease developed in guinea pigs kept on a diet of oats. The importance of this observation was not realized until several years had passed.

Nicolau noted changes of the skin and named them *scorbutides papulo-keratoziques folliculaires,* although there was no manifest scurvy. His early contribution is excellent.

Wiltshire noted involvement of the hair follicles in 87 per cent of 3,000 cases of scurvy observed in the Serbian army. Follicular hyperkeratosis was the first recognizable sign of the scorbutic tendency and permitted diagnosis before the onset of other scorbutic symptoms. The similarity to hyperkeratosis of the follicles in other states of malnutrition was recognized.

Nassau considered that punctate and larger ecchymotic spots on the face during the second year of life offered an early indication of lack of vitamin C.

Morawitz noted remarkable regression of pigmentary changes of the skin when a patient was given orange and lemon juice (vitamin C). He claimed a relation between the adrenal output and the intake of the vitamins in fruit juice. Morawitz advanced the concept of "pigment vitamins." Administration of vitamin C quickly eradicated the increased pigmentation of scurvy and of Addison's disease, and chloasma was successfully influenced by administration of vitamin C, according to the report.

Grüneberg reported excellent results from the administration of adrenal cortex rich in vitamin C in the treatment of arthropathic psoriasis. No relation was established between the adrenal cortex and the disease. Factors such as exposure to light were involved.

Daïnow found that l-ascorbic acid, or vitamin C, desensitized patients with arsphenamine or gold dermatitis. Others have reported similar observations.

Wilkinson and Ashford found that the degree of subnutrition of vitamin C, as determined by the method of Harris and Ray, paralleled the severity of Addison's disease.

Lutz (original reference not found) sought to determine the influence of ascorbic acid on psoriasis.

Pulay indicted lack of vitamins as the cause of psoriasis.

Daïnow reported inhibitory effects of l-ascorbic acid (vitamin C) on the virus of herpes and of zona.

Cornbleet, Klein and Pace reported the presence of from 0.55 to 0.64 mg. of vitamin C per hundred cubic centimeters of human sweat in normal persons—about the same proportion as in human blood serum.

Scheer reported a case of suspected scurvy in a woman who had subungual hemorrhages of all the fingers and the toes. The nails were lusterless and ridged but not scaly.

Cornbleet emphasized the increase in pigment in the skin when the depots of vitamin C in the adrenal glands and other parts of the body are depleted. Pigment and vitamin C occur together in the skin, the pigment anchoring the vitamin C. Copper is associated with vitamin C and with melanin in the skin and hastens the darkening and precipitation

of dopa by ultraviolet rays. Vitamin C retards this precipitation. The presence of copper, of vitamin C and of ultraviolet rays permits rapid change of the pigment. Lack of vitamin C accelerates production of pigment. Pigment once produced attracts and holds vitamin C.

Comment.—Patients with scurvy in New York city showed cutaneous lesions following the general description, ranging from petechiae to widespread ecchymoses, fissures and atonic ulcers. Multiple hemorrhagic extravasations of blood on the legs are usually grouped about the hair follicles, and variously sized areas of bluish black extravasations appear on the body spontaneously or after trauma. The knuckles become swollen, and in cases of severe involvement the skin and the subcutaneous tissue grow hard as a board. Stomatitis appears about the same time. The cause of the hemorrhages in the skin is fragility of the blood vessels.

The pigmentary phases of the activity of vitamin C are fascinating. It is difficult but essential that the relation between the effect of exposure to light of the vital or sunburning ultraviolet zone and that of such sensitizers as oil of bergamot be established. Copper plays some part, as in other effects of vitamin C.

VITAMIN D

Urbach claimed that no cutaneous lesions are caused by a deficiency in vitamin D.

Lucy and Devalin reported good results in the treatment of pemphigus with viosterol (vitamin D) in 6 cases.

Doktorsky and Platt reported improvement in acne vulgaris in 35 men and women between 17 and 30 years of age (including themselves) when vitamin D in the form of viosterol was administered. The pustules actually diminished by numerical count. Controls to whom administration of viosterol was stopped showed an increase in number of pustules.

Shelling and Asher noted that the hair of rats on a diet deficient in vitamin D grew poorly; some of the animals lost their long hair and were covered with thin fuzz. Other rats lost their hair in spots. Calcium and vitamin D in the food prevented this change in nearly all animals.

White presented cases in which ungual deformity in the form of irregular longitudinal ridging with slight transverse depressions or of marked atrophy was due to deficiency of vitamins B_2 and D. Proper diet caused cure.

Comel administered vitamin D to patients with eczema and reported improvement through fixation of the calcium in the tissue. There were marked increase of calcium in the blood and decrease of calcium in the urine. The lactic acid content of the blood decreased when vitamin D was given.

Excess of vitamin D in rabbits caused rough skin, shedding of the coat, calcification of the arteries in the skin and elsewhere and severe general symptoms.

The skin of children who were given vitamin D became brown. The skin of the back, the backs of the hands, the axillas and other regions exposed to light showed increase in pigmentation.

Ceder and Zon gave massive doses of crystalline vitamin D and viosterol (from 300,000 to 400,000 U. S. P. units of vitamin D daily) to a number of psoriatic patients. In 11 of 15, complete involution followed within from six to twelve weeks; 2 patients received some benefit, and 2 others no benefit. There was gradual recurrence of the psoriasis within from six weeks to five months in all but 4 patients, although the recurring lesions were not as severe as those preceding vitamin treatment. There were no untoward reactions during treatment, except clinical hypervitaminosis D with anorexia, nausea, malaise and urinary frequency in 3 patients, after ten or twelve weeks of treatment.

Comment.—Diverse problems are associated with the relation of the skin to vitamin D, its precursors cholesterol and physterol and the activating radiation of vital ultraviolet from the sun and effective artificial sources.

The possibility of cutaneous changes due to activated cholesterol is under discussion. There is a relation between cholesterol, calciferol and estrogen. These in turn are similar in ring structure to certain derivatives of dibenzanthracene which produce cancer on application to the skin. Tar-induced cancer is an experimental fact.

The exposure to vital ultraviolet sources which activate the precursors of vitamin D seems to be responsible for a long series of accidents to the living animal organism simultaneously exposed to such toxins as ergotized rye (animals) or chemicals like acetylsalicylic acid (human beings). The list of activating chemicals is growing. Mention of porphyrin recalls another series of cutaneous accidents associated with exposure to sunlight or to artificial sources of vital ultraviolet radiation. Histamine may be the intermediary in these cases.

VITAMIN E

Verzar and Kokas reported the cure of a disease of the hair of rats caused by deficiency of vitamin E through administration of anterior pituitary extract. The appearance of the diseased hair was similar to that caused by castration, being silky and woolly. The hair papillae became smaller, and the sebaceous glands were shrunken. The hair lost its elasticity with lack of vitamin E in experimental animals.

The existence of a relation between vitamin E and ovarian hormones is proposed. Further, it is reported that anterior pituitary gland substance may be effectively substituted for vitamin E.

VITAMIN F

Vitamin F, which has been extensively commented on recently, is said to prevent scaly skin on the rat's tail and other lesions similar to seborrhea. Vitamin F is linked to the unsaturated fatty acids of the type of linoelic acid.

Taub and Zakon used purified linseed oil in the treatment of eczema in a few selected cases. The results were so poor in 8 cases that the authors discontinued the use of the unsaturated fatty acid and concluded that the promiscuous use of linseed oil was entirely unjustified.

MISCELLANEOUS

Recent studies disclose the presence of vitamins A, C, D and possibly B_2 in the skin.

Maldan-Massot reported a case of typical acrodynia in a child of 20 months, who had been fed nothing but milk and pap. The child improved when placed on a diet of vegetables, meat juice, calf's liver and lemon juice. After eight days administration of vitamins A and D with thyroid and adrenal extracts was started. Another week passed, and all signs except tachycardia had disappeared. This case raised the question whether acrodynia is a deficiency disease.

Hall reported a case of dermatitis papillaris capillitii and sycosis vulgaris with evidence of avitaminoses A and D (night blindness). Improvement of the eruption followed feeding of cod liver oil.

Cohen discussed the case of a girl with ulcerative colitis, marked debility and pyoderma gangraenosum as an instance of vitamin deficiency.

SUMMARY

In the foregoing pages the characteristics of cutaneous lesions observed in experimental work with animals and in clinical practice with human beings which have been considered due to a lack or an excess of the individual vitamins have been outlined from the available literature. A few comments from my own experience have been added.

The bibliography is as complete as available sources have made possible. Nearly all the references have been checked back to the originals.

CONCLUSION

There is a growing literature on the dermatologic symptoms of vitamin deficiencies, and once more the axiom of the founder of the specialty is worth repeating: Dermatology includes the skin and everything inside it!

BIBLIOGRAPHY

Adams, P. D.: J. Biol. Chem. **116**:641, 1936.

Aykroyd, W. R.: Vitamins and Other Dietary Essentials, London, William Heinemann, Ltd., 1933.

Bloch, C. E.: Ugesk. f. læger **79**:1516, 1917. This article was not available.

Bodansky, M.: Introduction to Physiological Chemistry, ed. 3, New York, John Wiley & Sons, Inc., 1934.

Bridges, M. A.: Food and Beverage Analyses, Philadelphia, Lea & Febiger, 1935.

Busman, G. J., and Hegarty, F. A.: Subacute Follicular Dermatitis (Vitamin A Deficiency?), Arch. Dermat. & Syph. **34**:155 (July) 1936.

Ceder, E. T., and Zon, L.: Pub. Health Rep. **52**:1580, 1937.

Cohen, M. H.: Pyoderma Gangraenosum: A Deficiency Disease Complex, Arch. Dermat. & Syph. **33**:813 (May) 1936.

Comel, M.: Gior. ital. di dermat. e sif. **76**:89, 283 and 727, 1935.

Copping, A. M.: Biochem. J. **30**:845, 1936.

Cornbleet, T.: Avitaminosis or Scurvy, Arch. Dermat. & Syph. **29**:166 (Jan.) 1934.

Vitamin C and Pigment, ibid. **35**:471 (March) 1937.

——Klein, R. I., and Pace, E. R.: Vitamin C Content of Sweat, ibid. **34**:253 (Aug.) 1936.

Dainow: Ann. de dermat. et syph. **6**:830, 1935; **7**:817, 1936.

Dann, W. J.: J. Nutrition **11**:451, 1936.

Doktorsky, A., and Platt, S. S.: Vitamin D in the Treatment of Acne Vulgaris, J. A. M. A. **101**:275 (July 22) 1933.

Eddy, W. H., and Dalldorf, G.: The Avitaminoses, Baltimore, Williams & Wilkins Company, 1937.

Frazier, C. N., and Hu, C. K.: Cutaneous Lesions Associated with Deficiency in Vitamin A in Man, Arch. Int. Med. **48**:507 (Sept.) 1931.

Funk, C., and Dubin, E.: Vitamin and Mineral Therapy, New York, United States Vitamin Corporation 1936.

Gerstenberger, H. J.: Etiol and Treatment of Herpetic (Aphthous and Aphtho-Ulcerative) Stomatitis and Herpes Labialis, Am. J. Dis. Child. **26**: 309 (Oct.) 1923.

Giblin, W. E.: M. J. Australia **1**:202, 1936.

Goodman, H.: Arch. Pediat. **40**:372, 1938.

Copper as a Cause of Perfume Dermatitis and as a Suntan Stimulant, Arch. Dermat. & Syph. **34**:271 (Aug.) 1936.

——and Burr, M.: Juvenile Acrodynia: Brief Review of a Case Seen in New York, ibid. **23**:901 (May) 1931.

Goodwin, G. P.: Brit. M. J. **2**:113, 1934.

Grüneberg, T.: Arch. f. Dermat. u. Syph. **173**:1, 1935.

Guha, B. C.: Brit. M. J. **2**:53, 1931.

Gurin, S. S., and Eddy, W. H.: J. Exper. Med. **54**:421, 1931.

Hall, T. B.: Dermatitis Papillaris Capillitii and Sycosis Vulgaris with Hypovitaminosis, Arch. Dermat. & Syph. **33**:880 (May) 1936.

Hogan, A. G., and Richardson, L. R.: The Effect of Ultra-Violet Rays on the Dermatitis-Preventing Vitamin, Research Bulletin 178, University of Missouri, Columbia, Mo., December 1932.

Jadassohn: Ztschr. f. Vitaminforsch. **4**:324, 1935.

Jeghers, H.: The Degree and Prevalence of Vitamin A Deficiency in Adults, with a Note on Its Experimental Production in Human Beings, J. A. M. A. **109**:756 (Sept. 4) 1937.

Kuipers, F. C.: Nederl. tijdschr. v. geneesk. **75**:1108, 1931.

Lauber: Beitr. z. klin. Chir. **158**:633, 1933.

Loewenthal, L. J. A.: A New Cutaneous Manifestation in the Syndrome of Vitamin A Deficiency, Arch. Dermat. & Syph. **28**:700 (Nov.) 1933; Ann. Trop. Med. **29**:407, 1935.

Ludy, J. B., and Devalin, C. M.: Urol. & Cutan. Rev. **36**:817, 1932.

Mackay, H. M. M.: Arch. Dis. Childhood **9**:133, 1934.

Maldan-Massot: Bull. Soc. de pédiat. de Paris **31**:460, 1933.

Morawitz, P.: Klin. Wchnschr. **13**:324, 1934.

Mouriquand, G., and Gaté, J.: Verhandl. Internat. Kong. Dermat. **1**:256, 1937.

Müller: München. med. Wchnschr. **83**:2116, 1936.

Munella: Arch. Soc. de biol. de Montevideo **6**:229, 1936. This article was not available.

Nassau: Monatschr. f. Kinderh. **42**:593, 1933.

Nicholls, L.: Indian M. Gaz. **68**:681, 1933; **69**:241, 1934.

Nicolau, S.: Ann. de dermat. et syph. **7**:399, 1918.

O'Leary, P. A.: Northwest Med. **27**:319, 1928.

Osborne, T. B., and Mendel, L. B.: J. Biol. Chem. **15**:311, 1913.

Pallotti: Bull. d. sc. med., Bologna **3**:526, 1935.

Pasini: Verhandl. Internat. Kong. Dermat. **2**:166, 1937.

Pettler, M. F.: Pennsylvania M. J. **39**:864, 1936.

Pillat, A.: Does Keratomalacia Exist in Adults? Arch. Ophth. **2**:256 (Sept.); 399 (Oct.) 1929. Nat. M. J. China **15**:585 and 614, 1929.

Pulay: Bull. Soc. franç. de dermat. et syph. **43**:1508, 1936.

Radhakrishna Rao, M. V.: Indian J. M. Research **24**:727, 1937.

Redaelli, E.: Gior. ital. di dermat. e sif. **76**:765, 1935.

Reiss, F.: Chinese M. J. **50**:945, 1936.

Scheer, M.: A Case for Diagnosis (Subungual Hemorrhage Due to Vitamin C Deficiency?), Arch. Dermat. & Syph. **35**:522 (March) 1937.

——and Keil, H.: Follicular Lesions in Vitamin A and C Deficiencies, ibid. **30**: 177 (Aug.) 1934.

Sharples, L. R.: J. Trop. Med. **32**:358, 1929.

Sherman, H. C., and Smith, S. L.: The Vitamins, American Chemical Society Monograph Series, ed. 2, New York, The Chemical Catalog Company, Inc., 1931.

Smith, T., in Annual Report of the United States Department of Agriculture, Bureau of Animal Industry, 1895-1896, p. 172.

Sternberg, T. H., and Pillsbury, D. M.: The Influence of Avitaminosis A on Experimentally Produced Cutaneous Infection in Rats, Arch. Dermat. & Syph. **35**:247 (Feb.) 1937.

Sweet, L. K., and K'Ang, H. J.: A Clinical and Anatomic Study of Avitaminosis Among the Chinese, Am. J. Dis. Child. **50**:699 (Sept.) 1935.

Sweitzer, S. E.: Minnesota Med. **16**:670, 1933.

Szent-Györgyi: Deutsche med. Wchnschr. **58**:852, 1932.

Taub, S. J., and Zakon, S. J.: The Use of Unsaturated Fatty Acids in the Treatment of Eczema (Atopic Dermatitis, Neurodermatitis), J. A. M. A. **105**:1675 (Nov. 23) 1935.

Urbach, E.: Skin Diseases and Nutrition, Including the Dermatoses of Children, translated by F. R. Schmidt, Vienna, Wilhelm Maudrich, 1932.

Verzar and Kokas: Arch. f. d. ges. Physiol. **227**:511, 1931.

White, C.: Onychia Due to Chronic Hypovitaminosis, J. A. M. A. **102**:2178 (June 30) 1934.

Wilkinson, J. F., and Ashford, C. A.: Lancet **2**:967, 1936.

Wiltshire, H.: Lancet **2**:564, 1919.

LICHEN PLANUS OF LIPS

DOUGLASS W. MONTGOMERY, M.D.
SAN FRANCISCO

Lichen planus seldom appears on the lips and when it does usually the lower and not the upper is affected, and the eruption is almost always accompanied by lichen planus in the cheek pouches, a distinct aid in diagnosis.[1] The disease in this situation has several interesting peculiarities. For instance, although lichen planus is definitely papular, papules seldom appear on the lips. Furthermore, the exposed red is a semimucosa and is corneous, while the covering of the inner surface is similar to that lining the rest of the mouth and is not corneous. This causes a dissimilarity of the eruption in these two closely approximated surfaces. The confusion arising from this and other circumstances will be best elucidated by a discussion of individual cases.

REPORT OF CASES

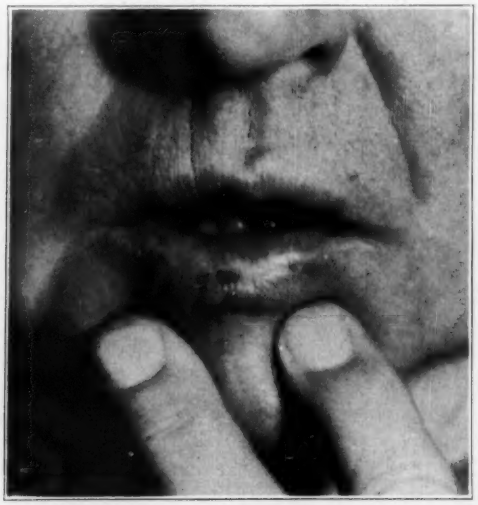
CASE 1.—The patient (fig.) was a strong, well built man, aged 68, who led an outdoor life. He was nervous, as those having lichen planus are apt to be. He had been under my care at intervals for over thirty years, suffering from various manifestations of his cutaneous trouble. When he consulted me on Nov. 8, 1937, he had patches resembling psoriasis on the legs and the forearms and well marked lichen planus of the scrotum. On the exposed red of the lower lip there was a white circle with a few formless white patches to its left. These lesions were obscured by rough, tightly adherent scales, giving to the affected surface a corneous quality. The most interesting lesions, however, were a number of white pointed streaks directed backward from the summit of the lip. They were beautifully delineated and contrasted in this respect with those of the exposed red, which was obscured. There were no lesions of lichen planus on the tongue or in the cheek pouches.

The milky whiteness of the lesions of lichen planus in the mucous membranes was due to a massive accumulation of keratohyalin in the thickened stratum granulosum. These milk white streaks and spots shone through the smooth, transparent covering of the mucous membrane, a characteristic symptom. The streaking was another matter. This frequently occurs in this disease after a traumatism, such as a scratch, but it also may follow the trend of the tissues. In the fetus the mouth extends far back, nearly to the ear as in a dog, and later grows forward, so that the trend of the tissues is forward toward a common center in the orifice

1. Juliusberg, F.: Lichen ruber und Pityriasis rubra pilaris, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 7, pt. 2, p. 33. Among 72 cases of lichen planus of the mouth and pharynx G. Trautmann (Die Krankheiten der Mundhöhle und der oberen Luftwege bei Dermatosen, ed. 2, Wiesbaden, J. F. Bergmann, 1911) observed 18 in which the lip was involved.

of the mouth. It has been said that these streaks follow the blood vessels, and they undoubtedly do, but the blood vessels constitute only a part of the tissues so directed.

CASE 2.—On May 4, 1936, a woman aged 69 consulted me for an extensive acute cutaneous eruption of lichen planus and an equally intense stomatitis with erosions and typical lesions like lacework in the cheek pouches. During the course of her disease a narrow eroded surface developed along the summit of the lower lip. This raw lesion slowly settled down to form a surface which looked as if recently cauterized with silver nitrate. Extending downward from the posterior border of this surface was a row of closely set fine white stripes shining through the polished transparent mucous membrane. These lines were exactly similar to those in case 1 and were so even in contour, length and distribution and ended in such sharp points that they gave the impression of being artificially delineated to represent conventionalized tongues of flame.



The illustration (case 1) shows the pointed streaks directed inward like tongues of flame (photographed by James D. Viecelli, M.D.).

CASE 3.—A man aged 39 consulted me on April 10, 1922, for hypertrophic lichen planus of the backs of the hands and of the legs. He had characteristic white circles and streaks in the pouch of one cheek and a leukoplakia-like thickening of the glans penis. The exposed red of the lower lip was occupied by a scaly white crust. At the upper border of the dry scaly band was a zone in which the red of the lip was stippled with white points. This tightly adherent crust might have been mistaken for lupus erythematosus—hence the value of the "white stippling" in fixing the diagnosis.[2] In this case the association of this type of eruption on the lip with a leukoplakia-like thickening of the semimucosa of the

2. J. A. Fordyce and G. M. MacKee (Clinical Types of Lichen Planus, J. Cutan. Dis. **37**:320 [May] 1919) have drawn attention to this strange absence of papules and to the occasional formation of a tightly adherent crust resembling that of lupus erythematosus.

glans penis was interesting; it might have been due to some special tendency which caused his tissues to react in this manner to the virus, whatever it may be, of lichen planus.

Case 4.—A similar picture was presented by a man aged 44, who consulted me on Sept. 16, 1915, for lichen planus of the anterior surface of the right leg. He had beautifully delineated small papules with white tops in both cheek pouches, and the exposed red of his lower lip was covered with white, tightly adherent scales.

Case 5.—A man aged 67 consulted me on June 30, 1913. He weighed 172 pounds (78 Kg.) and was manifestly overnourished. Besides his cutaneous eruption he had lichen planus of the tongue, the cheek pouches and the anus and a white ring on the exposed red of the lower lip.

Case 6.—A man aged 37 consulted me on April 28, 1909, for extensive lichen planus of the skin. I noted in the history only that he had lichen planus of the lower lip and that it felt heavy. He had a decided tendency to this eruption of the mucous membranes, as he had white flattened polished papules on both sides of the dorsum of the tongue and a white raised circinate lesion in one cheek pouch opposite the last molars. He had papules of lichen planus on the glans penis and what appeared to be eczema ani but probably was lichen.

Case 7.—A physician aged 57 consulted me on Sept. 21, 1922, for one of the most beautifully marked, large flat papular violet-colored eruptions on the bearded area of the face that I have ever seen. Besides this he had lichen planus of the scalp, the cheek pouches and the anus and characteristic white lacework of the exposed red of the lower lip.

Case 8.—A papular eruption is rarely seen on the lips in this disease, but when it does occur the papules may be profuse. Such was the case of a girl aged 15 whom I saw on Aug. 17, 1936. She had hypertrophic papules of lichen planus on the legs which resembled verrucae, and there were well marked lesions of lichen planus in the cheek pouches, of which, as is usually true, she was unaware. A row of these papules ran along the interdental line to the right corner of the mouth and then divided, one branch running along the summit of the upper and the other along the summit of the lower lip for about a centimeter. These rows were composed of definite closely set sodden white papules. Occasionally the lips may be definitely and extensively papular, as in a case presented by Kren [3] before the Vienna Dermatological Society in which the red of both lips was beset by closely set papules.

Often a definite ridge runs anteroposteriorly along the internal surface of each cheek at the level of the closure of the upper and the lower denture. The crest of this ridge is naturally white, and from its whiteness and its linearity it may be mistaken for a streak of lichen planus. This line may indicate the line of growth of the fetal mouth from behind forward, previously mentioned, or it may arise in a person who has soft mucous membranes which protrude between the bite of the teeth. I have called this the interdental line. In the young girl mentioned in case 4 this line was especially well marked, and it was beset with papules, making it in this case a line of lichen planus as well

3. O. Kren (Arch. f. Dermat. u. Syph., Jan. 15, 1912) reported a case of extensive lichen planus with closely set papules of the red area of the lips.

as an interdental line. This interdental line has been called an intercalary line, from *intercalare* (to put something between),[4] which has the same meaning. It has also been called the raphé buccalis, an excellent designation recalling its developmental origin.[5]

CASE 9.—A Japanese woman aged 37 who had extensive lichen planus of the skin acquired an excoriated line along the summit of the lower lip which I regarded as due to the same disease. This lesion exactly resembled the narrow eroded line running along the summit of the lower lip mentioned in case 2. Its even breadth, its straight borders and its artificial appearance all suggested lichen planus.

CASE 10.—A mining man aged 42, whom I saw in October 1914, had a foul mouth, with a greenish coating on the lower gums and a collection of pus on the lips every morning, which I took to be an active manifestation of lichen planus.

CONCLUSIONS

The lips seldom become papular in cases of lichen planus. The lesions of this disease on the lips resemble those occurring in the mouth as white stripes, rings, stars, lacework and dots shining through the upper layers of epithelium. The lips are covered with two kinds of epithelium, of which that covering the exposed red is corneous, so that when its cells are incited to overaction they tend to adhere, obscuring the deeper, milk white lesions and even forming tightly adherent crusts. The inflammatory reaction may be more active and cause an erosion, and this erosion may run along the top of the lip as an even band, or it may be still more intense and cause extensive cheilitis with a heavy purulent discharge.

---

4. Juliusberg,[1] p. 28.

5. Pinkus: Die Normale Anatomie der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 1, pt. 1, p. 296.

"ACNE MIXED" UNDENATURED BACTERIAL ANTIGEN IN TREATMENT OF ACNE VULGARIS

MAURICE J. COSTELLO, M.D.
AND
J. CHARLES WASHBURN, M.D.
NEW YORK

Numerous types of acne vaccine have been tried for years in the treatment of acne vulgaris. The results have been poor or indifferent. Enthusiastic claims were soon proved to be unfounded. It is the consensus of practitioners who treat this condition in many cases that vaccines are worthless. The good results claimed by the manufacturers of acne vaccines prompted us to use such treatment again in a series of cases at the Bellevue Hospital. We employed an "acne mixed" undenatured bacterial antigen prepared according to Krueger's [1] method in the treatment of this most common of cutaneous diseases. In a previous experiment Kindel and one of us (M. J. C.) [2] failed to obtain good results in the treatment of pustular dermatoses, including acne vulgaris, with staphylococcus toxoid-Lederle N. N. R.

In the current experiment the patients were given injections of the vaccine twice a week. They were observed by both of us and by other members of the staff at each visit to the outpatient department. Both the pustular and the papular type of acne were treated. Cases were grouped according to severity, duration and extent of the condition as mild, moderate and severe. Forty patients were treated, 23 of whom were males and 17 females, the age varying from 15 to 24 years. About one quarter of the patients used iodized salt, and 10 of the total number had taken yeast, which had frequently aggravated the condition.

In this "acne mixed" undenatured bacterial antigen, merthiolate 1:50,000 was used to devitalize the cultures and to allow the minimum amount of alteration of proteins.

Krueger,[1] according to the manufacturer, has described a method for the preparation of bacterial antigens which does not require the use of

---

From the Service of Dermatology and Syphilology, Bellevue Hospital, Service of Drs. Howard Fox and E. R. Maloney.

The antigen used was supplied by Eli Lilly & Co.

1. Krueger, A. P.: A Method for the Preparation of Bacterial Antigens, J. Infect. Dis. **53**:237, 1933.

2. Kindel, D. J., and Costello, M. J.: Staphylococcus Toxoid in the Treatment of Pustular Dermatoses, J. A. M. A. **102**:1287 (April 21) 1934.

heat or chemical or biologic treatment. The bacteria are grown in mass cultures, washed in buffered isotonic solution and then ground in a ball mill which, it is claimed, mechanically fragments the living bacteria. Residual intact cells are removed by ultrafiltration. The resulting filtrate contains the fragmented bacterial cells thrown into solution or suspension by physical rupture of the cell membrane. The final product is then standardized by means of its nitrogen and its protein content. It is claimed that better results would follow the use of the undenatured bacterial antigen produced by this method, which strictly avoids heat. (Mixed undenatured bacterial antigen Krueger contains Staphylococcus and the acne bacillus).

Results of Treatment

Type of Acne	No. of Cases	Degree of Acne			Total Average Dose (Cc.)	Maximum Total Dose (Cc.)	Condition After Treatment		
		Mild	Moderate	Severe			Improved	Unimproved	Worse
Papular	17	1	4	0	13	17	0	0	5
Pustular	23	5	12	18	13	17	0	35	0

From the table it can be understood readily why it was so difficult to persuade patients to continue with this treatment. Of the 40 patients treated, 35 were unimproved and 5 were definitely worse. The patients were treated for about four months, no other form of therapy being given.

The vaccine was administered by subcutaneous injection twice a week. The initial dose was 0.1 cc., increased by 0.1 cc. at each visit until a dose of 1 cc. was reached. The maintenance dose was kept just below that which gave a reaction (more than 1 cc. in over half the cases).

The local reactions on the whole were mild. When they occurred they consisted of erythema and slight swelling measuring 2.5 by 8 cm. which remained for from twenty-four to forty-eight hours. The patients had been treated at the clinic by topical applications for a period before the vaccine therapy was instituted.

SUMMARY AND CONCLUSIONS

An undenatured bacterial antigen prepared by Krueger's method was used in the treatment of acne vulgaris. The patients received an average of sixteen injections and a total average dose of 13 cc. In no instance was a patient improved, and 5 were made worse. No one has as yet proved that vaccines or toxoids are of any value in the treatment of acne vulgaris. Our results strikingly parallel those of other investigators of vaccines.

DERMATITIS GANGRAENOSA INFANTUM

MAURICE L. BLATT, M.D.

CHARLES K. STULIK, M.D.

AND

ADOLPH NACHMAN, M.D.

CHICAGO

Dermatitis gangraenosa infantum is one of the rare but serious cutaneous diseases of childhood. In the past fifteen years three cases have been reported in English and American dermatologic literature, while the pediatric literature over this same period has contained no mention of it. Recently a child with this condition came under our observation. The unusually extensive involvement of the skin, the presence of staphylococcic bacteremia and the apparent response to intensive treatment, followed by complete recovery, prompts us to report the case.

The lesions of dermatitis gangraenosa infantum begin as discrete papules and soon develop into pustules. A scab forms, with ulceration at the periphery, and there may be surrounding hyperemia. The eschar is usually black; when it is removed, ulcers with sharp perpendicular edges are revealed. These vary in diameter up to several centimeters. They look as if different-sized holes had been punched out. The entire thickness of the skin is involved, and there is usually a purulent discharge. Preceding the appearance of the lesions there may be nondescript erythema. The ulcers may appear on any part of the body. As in variola, a localizing factor, apparently, is irritation of a part of the cutaneous surface; in our case the abdomen and the chest were most involved because to protect his eyes from the light the child lay on his abdomen. Leukocytosis and high fever are usually present. Localized pulmonary abscesses, as well as pleural and pericardial empyema, have been noted. Cultures of blood may or may not show organisms.

REPORT OF A CASE

K. F., a boy aged 2 years and 11 months, was admitted to the Children's Division of the Cook County Hospital on June 3, 1937, because of photophobia, discharge from both eyes and an eruption of about three weeks' duration.

The child had been in apparently good health until three weeks before admission. At that time the mother noted the first symptom, a rash located predominantly on the scalp, behind the ears and on the upper lip, with occasional scattered lesions on the trunk and the extremities. The lesions were blister-like

From the Children's Division, the Cook County Hospital.

and when broken discharged a yellowish material. The general condition at that time, the mother reported, was excellent. On examination shortly before in an outpatient clinic for persons with cutaneous disease, the lesions were described as "multiple, discrete, moist and crusted, varying in size up to that of a dime and distributed chiefly on the scalp and behind the ears, with occasional pinpoint-sized maculopapules on the trunk and the dorsum of the forearm." A diagnosis of seborrheic eczema with secondary impetiginization was made. Several days after the cutaneous lesions were noted, the child complained of burning and itching of the eyes and preferred to keep his eyes closed. Because of this he was taken to the ophthalmologic clinic at Rush Medical College, where a diagnosis of phlyctenular keratoconjunctivitis was made. Failure of the eyes to respond to treatment, coupled with a progression of the cutaneous lesions and the development of signs of toxemia, prompted the clinic to advise hospitalization in our ophthalmologic department, from which he was promptly transferred to the children's division because of his serious condition.

Fig. 1.—Dermatitis gangraenosa infantum of seven weeks' duration.

Past History.—The patient had been born at term, when he weighed 9 pounds 5¼ ounces (4,231 Gm.). He had been breast and bottle fed for eight months and had received cod liver oil regularly but orange juice only on occasion. At the age of 1 year he had had whooping cough and at 1½ years a cold that lasted for four weeks.

Family History.—The mother had been in a sanatorium for tuberculous patients for nine months, three years prior to his birth. During the intervening years she had been followed at a municipal dispensary for patients with tuberculosis, where collapse therapy had been instituted. Her condition was classed as far advanced arrested tuberculosis. Because of the known tuberculous contact a roentgenogram of the child's chest was taken in September 1934. A diagnosis of healing tuberculosis of childhood type was made. On subsequent visits to the clinic satisfactory progress was recorded.

Physical Examination.—The patient was moderately emaciated, poorly developed and acutely ill. The temperature was 101 F., the pulse rate 130 and the respiratory rate 20. By preference the child lay on his abdomen and shielded his eyes from the light. The ophthalmologic department reported "marked redness and swelling of all four eyelids, associated with blepharospasm and photophobia. The margins of the lids were crusted and agglutinated by a whitish mucopurulent material, which oozed out of the conjunctival sac when the lids were separated. The palpebral conjunctiva was hypertrophic, edematous and intensely hyperemic. The bulbar conjunctiva showed deep mixed injection. The extraocular movements were normal. Both corneas revealed macroscopic vascu-

larization from all points along the circumference of the limbus. There were several old phlyctenular opacities, with several areas of recent infiltration and ulceration. The conjunctival vessels passed to these phlycentenulae and reached the central corneal area. The posterior segment and the lens could not be visualized."

The scalp, the ears and both lips were the sites of hyperemic, crusted vesicular lesions, with a purulent secretion completely occluding both nares. The upper lip was so edematous and indurated that opening of the mouth was almost impossible. Over the entire scalp and the face were multiple sharply defined punched-out ulcerations. The oral mucosa was free from lesions. Bilateral cervical adenopathy was noted. The heart and the lungs were apparently normal. The abdomen was soft, and the liver, the kidneys and the spleen were not palpable. The entire surface of the body, especially the anterior portion of the chest, the abdominal wall and the sacral area, was dotted with papuloulcerative lesions. Some of these lesions were merely papules; some were scabbed with a black tough eschar; some were ulcerated, and some were punched-out lesions with perpendicular edges which involved the entire thickness of the skin. The bases of these ulcers were necrotic and covered with pus. A few lesions had healed with definite scar formation.

Laboratory Findings.—The Wassermann and the Kahn reaction were negative. During the acute illness Mantoux tests with 1:100 dilution gave negative results, while during convalescence tests with 1:10,000 dilution of Koch's old tuberculin produced a strongly positive reaction. Repeated examinations of the blood showed values between 55 and 78 per cent for hemoglobin, 3,500,000 and 5,000,000 for red blood cells and 3,500 and 5,000 for white blood cells. The differential count was essentially normal. Repeated examinations of the urine showed no abnormalities. Cultures of pus from the lesions revealed hemolytic Staphylococcus aureus. The same organism was found in cultures of blood on three occasions.

The ascorbic acid content of the blood (determined by the method of Farmer and Abt) ranged from 0.4 mg. per hundred cubic centimeters of blood during the acute illness to 0.57 mg. (normal 0.7 mg.) during convalescence. Roentgenograms of the chest taken during convalescence revealed diffuse infiltration in the right pulmonary field, with marked calcification of the hilar lymph nodes. On three occasions stomach washings showed no tubercle bacilli.

Course.—During the first five weeks of the child's stay in the hospital his condition became progressively worse. New ulcers continued to form during this period. The ulcers on the abdomen and the sacrum enlarged and in some areas became confluent. There was lysis of the skin between the lesions, and raw necrotic areas, the largest being 10 by 15 cm., appeared on the anterior part of the abdominal wall and the sacrum.

After the fifth week of hospitalization the temperature, which had remained between 102 and 104 F., fell to a lower range; the infection subsided, and the lesions began to heal, leaving scars resembling pockmarks. The discharge from the eyes gradually decreased; photophobia became less prominent, and healing slowly took place, with the formation of several small corneal opacities which apparently do not interfere with distant vision. The patient's appetite improved and by Aug. 21, 1937, his weight had increased to 35 pounds (15.9 Kg.), 11 pounds (5 Kg.) more than his weight prior to the onset of his illness. Roentgenograms revealed a reduction in the size of the infiltration of the right pulmonary field.

Treatment.—Hot dressings were applied to the eyes every four hours. Irrigations with solution of boric acid were used as often as needed to keep the conjunctival sac free of secretion, and 1 per cent solution of atropine was instilled twice daily. At the onset colloid baths and local applications of 2 per cent ammoniated mercury were used, with no apparent success. Mindful of the excellent results reported from the use of solution of urea in the treatment of other

Fig. 2.—Appearance of child three and a half months later.

chronic purulent infections,[1] we applied wet dressings of a 25 per cent solution of this salt to the ulcerating lesions every two hours day and night. In two weeks the lesions were nearly clean, and there was no longer any drainage. Healthy granulation and healing began. At this stage the lesions were painted with a 1 per cent solution of methylrosaniline until crusts formed. Under

1. Robinson, W.: Use of Urea in Chronic Purulent Wounds, Am. J. Surg. **33**:192, 1936.

these crusts epithelization of the large ulcerated areas gradually took place. In the later stages of the healing process the placing of adhesive strips over the granulating areas aided healing.

Multiple small blood transfusions were administered to combat septicemia and a liquid diet high in calories and vitamins was given. Because of the low level of ascorbic acid in the blood 100,000 units of pure ascorbic acid was given over a period of forty-eight hours. This was coincident with the local treatment with carbamide. After this 8 ounces (0.24 liters) of orange juice was given daily. Under this regimen the patient made slow but steady progress to complete recovery.

COMMENT

Dermatitis gangraenosa infantum was first described by Stokes [2] in Ireland in 1880. In his case the condition followed vaccinia. In 1882 Hutchinson [3] in England noted the condition, calling it varicella gangraenosa. Crocker [4] in 1887 described the condition so completely and so accurately that his report has been the basis for most of the subsequent papers on the subject. It was his impression that the lesions were "pathological accidents," which with young children, especially of tuberculous constitution, might supervene on any pustular lesion, although they commonly followed varicella. He described three general forms of the disease: the first following varicella; the second having no preceding varicella, and the third occurring subsequent to vaccinia. In six of the twelve cases he reported the condition developed spontaneously in a child under 3 years of age; in two it followed vaccination, and in four it followed varicella. According to Crocker, the lesions may be few, with a good prognosis, or they may be numerous and extensive and result in death. Subsequent reports have appeared in the literature from time to time under different titles: pemphigus gangraenosa (H. Stokes), *ecthyma infantile gangréneux* (Pineau), multiple cachectic gangrene and rupia escharotica. The disease has been noted to complicate whooping cough, scarlet fever, measles, chickenpox, smallpox, vaccinia and purpura,[5] and it has occurred independent of any preceding illness.

The etiology of this type of disseminated gangrene of the skin is uncertain. Some investigators have expressed the thought that there was a bacterial causation; a toxic basis has been considered by others, while more recently it has been postulated that allergy may play a role. In

2. Stokes, A.: A Case of Vaccinia Gangrenosa, Dublin J. M. Sc. **69**:497, 1880.

3. Hutchinson, J.: On Gangrenous Eruptions in Connection with Chicken-Pox and Vaccination, abstracted, Proc. Roy. M. & Chir. Soc., London **9**:88, 1882.

4. Crocker, H. R.: Dermatitis Gangrenosa Infantum, Brit. M. J. **1**:1333, 1887.

5. Dwyer, H. V., and Klinkerfuss, G. H.: Dermatitis Gangrenosa Infantum, Arch. Dermat. & Syph. **11**:368 (March) 1925. Morrissey, M. J., and Reynolds, H. S.: Dermatitis Gangrenosa Infantum, ibid. **22**:811 (Nov.) 1930.

view of the more recent knowledge concerning the relation of vitamin C deficiency to infection, the possibility of this as an etiologic factor must be considered.

A variety of organisms have been recovered from the lesions, namely, Staphylococcus, Streptococcus, Bacillus pyocyaneus,[6] Salmonella Bacillus suipestifer [7] and diphtheroids. Dudden [8] reported four cases of fatal termination in which B. pyocyaneus was isolated. From autopsy in his cases he could not be sure whether the infection was endogenous (in two cases cultures of blood gave positive results) or whether there was exogenous infection with subsequent invasion of the blood stream. Because of the punched-out character of the lesions in our case, we believe that after the primary cutaneous infection an invasion of the blood stream occurred in which embolic manifestations involved the terminal arterioles of the skin, with resultant septic infarcts. The persistently positive results of cultures of blood seem to be in favor of this thesis; however, we were never able to demonstrate localization of staphylococci in organs other than the skin.

Pasachoff and Sobel [9] reported a case in which the condition developed three weeks after the onset of scarlet fever and suggested a possible allergic cause for the ulcerations. They suggested the possibility that this disease represents a clinical manifestation of the phenomenon of local cutaneous reactivity in experimental animals, which was described by Shwartzman.[10] This phenomenon presupposes an original sensitization of the skin and subsequent contact with the sensitizing antigen, resulting in gangrene of the sensitized areas. Schreus and Goehl [11] reported cases in which a papular erythematous rash accompanied a local pyodermic infection and disappeared after healing of the original focus. In the two cases they described, there was complement fixation with staphylococcus antigen. Other authors, however, have been unable to determine that patients with dermatitis gangraenosa show definite reactions against bacteria or their filtrates.

Malnutrition, cachexia and constitutional inferiority are definitely predisposing factors. Although Crocker stated that affected children

---

6. Hitschmann, F., and Kreibich, K.: Pathogenicity of B. Pyocyaneus and the Etiology of Ecthyma Gangrenosum, Wien. klin. Wchnschr. **10**:1093, 1897.

7. Hu, C. K.: Dermatitis Infantum Gangrenosum, Nat. M. J. China **15**:149, 1929.

8. Dudden, E.: Ecthyma Gangrenosum, Jahrb. f. Kinderh. **9**:257, 1922.

9. Pasachoff, H. D., and Sobel, N.: Dermatitis Gangraenosa Infantum in the Course of Scarlet Fever, Arch. Dermat. & Syph. **26**:428 (Sept.) 1932.

10. Shwartzman, G., cited by Pasachoff and Sobel.[9]

11. Schreus, H. T., and Goehl, E.: Ueber lichenoide Eruption (lichen pyodermicus) nebst Bemerkungen über Komplementablenkung im Blute bei Staphylocokken und Trichophytie-Ergrangungen mit Berücksichtigung der Einwirkung von Röntgenstrahlen, Dermat. Ztschr. **31**:273, 1920.

are often tuberculous, reports of other authors do not substantiate this. What relation, if any, existed between the childhood tuberculosis in our case and the cutaneous lesions is questionable. With the manifestation of tuberculous allergy as phlyctenular keratoconjunctivitis and a strongly positive reaction to the Mantoux test, the possibility that the underlying lesion was a papulonecrotic tuberculid must be considered. Such tuberculids, however, usually appear on the extremities and face and only occasionally on the abdomen and the back and are usually much smaller than those observed in our case.

Kux [12] described a case of disseminated tuberculid associated with miliary pulmonary tuberculosis in an infant of 6 months. There was a general distribution of lesions with concentration and aggravation about the lower part of the abdomen and the diaper area. The lesions consisted of hemorrhagic blebs, with residual ulcerating craters up to several centimeters in diameter. Kux called the condition exanthemic tuberculid because of its resemblance to varicella and in contradistinction to localized lupus vulgaris or tuberculosis verrucosa cutis.

It is interesting to postulate the possible relation between vitamin C deficiency and pyoderma. Was the hypovitaminosis, indicated by the low blood content of the ascorbic acid, a contributing factor (a partial depletion of one of the factors necessary for normal vitality of the skin) or merely an incidental finding, or were the lesions a manifestation of generalized scurvy? Small petechial nodules (acne scorbutica), small vesicles filled with a sanguinolent fluid (herpes scorbuticus) and large vesicles filled with a bloody fluid (pemphigus scorbuticus) have all been described in cases of scurvy.[13] In some cases these have ulcerated. The ulcers have become covered with a brownish red or black eschar, which when removed leaves a foul necrotic base. In these cases of scorbutic cutaneous lesions other manifestations of scurvy not noted in our case were present.

The prognosis is dependent on a number of factors. In general, a large number of lesions, especially if accompanied by evidences of septicopyemia, makes the prognosis grave. The younger the child, the more serious the outlook. In common with all other infections, prognosis is dependent, in part at least, on intensity of treatment.

The important elements in therapy are combating the cutaneous infection, maintaining nutrition and coping with the septic state.

---

12. Kux, A.: Disseminated Tuberculosis of the Skin in an Infant, Bratisl. lekár. listy **16**:29, 1936.

13. Howard, C. P., and Mills, E. S., in Christian, H. A., and Mackenzie, J.: Oxford Medicine, New York, Oxford University Press, 1928, vol. 3, p. 161.

SUMMARY

A case of dermatitis gangraenosa infantum in a 3 year old child is reported. Hemolytic Staph. aureus was cultured from the lesions and the blood stream. Recovery ensued despite extensive involvement of the skin and in spite of repeatedly positive blood cultures. Hypertonic solution of carbamide was used locally, and the vitamin intake increased with apparent success. Multiple small blood transfusions seemingly aided in maintaining nutrition and overcoming sepsis.

RELAPSING FEBRILE NODULAR NONSUPPURATIVE PANNICULITIS (WEBER-CHRISTIAN DISEASE)

REPORT OF TWO CASES

LORETTA JOY CUMMINS, M.D.
AND
WALTER F. LEVER, M.D.
BOSTON

Two cases of relapsing febrile nodular nonsuppurative panniculitis were observed at the Massachusetts General Hospital in 1937, and because the number of known cases is so small, it was thought advisable to report them.

The characteristic feature of this disease is the recurrence of crops of subcutaneous nodules which either remain separate or become, by confluence, indurated areas of subcutaneous fat. They are usually tender and painful. Malaise and slight fever accompany the appearance of nodules in most cases. The pathologic changes are necrosis of the subcutaneous fat and later inflammation and fibrosis. Usually complete removal of the fat follows, resulting in a sharply circumscribed area of depressed skin. Some nodules, especially the smaller ones, may disappear without leaving any trace. As a rule, no pathologic changes are observed in other parts of the body. In a few cases an enlarged spleen and leukopenia have been reported.

The diagnosis of relapsing febrile nodular nonsuppurative panniculitis is easily made. The initial nodules may be similar to those of erythema nodosum, erythema induratum or subcutaneous sarcoid of Darier and Roussy, but in none of these diseases are the nodules followed by atrophy of the subcutaneous fat without change in the skin. Adiposis dolorosa (Dercum's disease) may exhibit lipomas resembling the nodules of relapsing febrile nodular nonsuppurative panniculitis, but the nodules in Dercum's disease remain unchanged for years, without undergoing any atrophy. In any case a biopsy will prove the diagnosis. The morphea type of scleroderma is characterized by an induration of the corium which is plaquelike and not nodular. Dermatomyositis extends over larger, less sharply circumscribed areas; movements are extremely painful, and there is muscular weakness. The chief pathologic

From the Department of Dermatology and Syphilology of the Massachusetts General Hospital.

changes in dermatomyositis are in the muscles, which are not involved in Weber-Christian disease.

Accounts of 13 cases of relapsing febrile nodular nonsuppurative panniculitis have been published up to the present time. The first case was described by Pfeifer [1] in 1892 under the name *"herdweiser Atrophie des subcutanen Fettgewebe."* His patient, a 23 year old woman, for two years had crops of subcutaneous nodules, with resultant atrophy of the fatty layer. The lesions were spread diffusely over the body. The second case was reported in 1916 by Gilchrist and Ketron.[2] In their patient, a girl 8 years old, only the lower extremities were involved. Weber [3] reported the third case, that of a woman 50 years old, who had diffuse lesions on the trunk and the extremities. In 1928 Christian,[4] reporting the fourth known case, gave the disease its present name. His patient, a woman 22 years old, had ten attacks within ten years. The first manifestation was on the right arm, and during the ensuing attacks nodules cropped out on all parts of the body except the head, the hands and the feet. A remarkable feature in Christian's case was the temperature, which during some attacks rose to 104 F. The time between attacks varied from a few months to two years. In 1933, 3 more cases of the disease were reported: 1 by Alderson and Way,[5] 1 by Netherton [6] and a third by Weber.[7] An eighth case was reported by Brill [8] in 1936. Bailey [9] in 1937 added 5 more cases to the literature. Previous to that time, the patient in all reported cases was a woman, but Bailey reported the condition in a man. One of his patients had a continuous fever, the temperature usually not falling below 100 F. and rising in the

1. Pfeifer, V.: Ueber einen Fall von herdweiser Atrophie des subcutanen Fettgewebe, Deutsches Arch. f. klin. Med. **50**:438, 1892.

2. Gilchrist, T. C., and Ketron, L. W.: A Unique Case of Atrophy of the Fatty Layer of the Skin, Preceded by the Ingestion of the Fat by the Large Phagocytic Cells—Macrophages, Bull. Johns Hopkins Hosp. **26**:291, 1916.

3. Weber, P. F.: A Case of Relapsing Non-Suppurative Nodular Panniculitis, Showing Phagocytosis of Subcutaneous Fat Cells by Macrophages, Brit. J. Dermat. **37**:301, 1923.

4. Christian, H. A.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, Arch. Int. Med. **42**:338 (Sept.) 1928.

5. Alderson, H. E., and Way, S. C.: Relapsing Febrile Nonsuppurative Panniculitis (Weber), Arch. Dermat. & Syph. **27**:440 (March) 1933.

6. Netherton, E. W.: Relapsing Nodular Nonsuppurative Panniculitis, Arch. Dermat. & Syph. **28**:258 (Aug.) 1933.

7. Weber, F. P.: A Further Note on Relapsing Febrile Nodular Non-Suppurative Panniculitis, Brit. J. Dermat. **47**:230, 1933.

8. Brill, I. C.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), in Medical Papers Dedicated to Henry Asbury Christian, Baltimore, Waverly Press, Inc., 1936, p. 694.

9. Bailey, R. J.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), J. A. M. A. **109**:1419 (Oct. 30) 1937.

afternoon to between 101 and 105 F. This patient died fourteen months after the onset, but it has not been conclusively established that Weber-Christian disease was the immediate cause of death, as the patient died at home and no necropsy was done.

The cause of the disease is unknown. There are no definite indications that bacterial infection is a factor. Cultures of the blood and of material from the lesions always gave negative results. Focal infections of teeth and tonsils were observed in the 5 cases reported by Bailey. In Weber's second case and in Bailey's 5 cases, ingestion of bromides or of iodides was recorded; 1 patient of Bailey's had a recurrence after administration of iodides and a remission when the drug was discontinued. Both patients reported on in this paper denied having taken iodides or bromides. Bailey expressed the belief that drugs, particularly iodides, may be a precipitating factor. Injections of insulin,[10] of camphor in oil [11] and of paraffin [12] can lead to a fat necrosis which, to a great extent, resembles the pathologic picture of relapsing febrile nodular nonsuppurative panniculitis. In all the cases referred to, however, the fat necrosis was a foreign body reaction. Gilchrist and Ketron expressed the opinion that in Weber-Christian disease an unknown cause leads to a change in the subcutaneous fat; the metamorphosed fat acts then as a foreign body and calls forth a foreign body inflammatory reaction. There is no indication of any disturbance in the fat metabolism. The lipoid fractions of the blood were studied in 1 of the cases reported in this paper and were all well within normal limits.

REPORT OF CASES

Case 1.—A 10 year old girl was admitted to the dermatologic department of the Massachusetts General Hospital on May 11, 1937. The family and the past history were irrelevant. Late in February 1937, she had first noticed a painless "lump under the skin" on the lateral aspect of the lower part of the left leg. This nodule was not elevated and could be felt only by pressure. It was the size of a lima bean and was at no time tender; it did not enlarge. A week after its appearance the lump seemed to disappear ("to become lost") in a rapidly developing "dent" in the skin of this region. The depression was never tender and showed no signs of inflammation; it grew rapidly to the size of a silver dollar and remained that size until early in May 1937. Late in March 1937 a similar depression developed on the outside of the left thigh, but without an antecedent lump at that site and again without pain, tenderness or redness. This depression rapidly increased to 6 by 6.5 cm. and remained unchanged. Late in April, two weeks before admission, the patient noticed a lump deep in the skin on the back

10. Avery, H.: Insulin Fat Atrophy: A Traumatic Atrophic Panniculitis, Brit. M. J. **1**:597, 1929.

11. Henschen, K.: Ueber subcutane Fremdkörpergeschwülste aus nicht resorbierten Kampferölinjectionen (Oelgranulome), Zentralbl. f. allg. Path. u. path. Anat. **25**:417, 1914.

12. Stokes, J. H., and Scholl, A. J., Jr.: A Case of Probable Paraffin-Oil Tumor, Arch. Dermat. & Syph. **4**:50 (July) 1921.

of the leg, 5 cm. above the malleolar line. This was the size of a lima bean and was symptomless. The nodule was followed by depression of this area six days later. At this time the first depression, on the middle part of the leg, showed an erythematous border, and it seemed to be enlarging at the time of admission. No history of elevation in temperature or of ingestion of drugs could be obtained.

Physical examination showed the girl to be in excellent health. On the left leg there were three areas in which the skin showed retraction to a depth of 1 or 1.5 cm., one on the outer surface of the middle part of the thigh, one on the outer

Fig. 1 (case 1).—Appearance of leg in May 1937. Two of the three indentations, one on the thigh and one on the leg, are visible.

surface of the leg, just below the belly of the gastrocnemius and one on the back of the leg, 5 cm. above the malleolar line. All three depressions were about the size of a silver dollar. In these areas the skin was slightly coarser, owing to keratosis of the follicular openings. Around the lesion on the outer side of the leg there were slight redness and a thicker than normal rim. Just above the area on the back of the leg there was a firm walnut-sized nodule deep in the skin, demonstrable only by palpation. This was not sharply demarcated from the surrounding tissue and was slightly tender. There was no apparent disturbance of sensation in any of these areas. The teeth showed much tartar, and the left upper bicuspid was carious.

The temperature was normal during the time of observation in the ward. Roentgenograms of the chest and the bones showed no abnormality. The blood picture was normal on several occasions. Chemical analysis of the blood (including determinations of nonprotein nitrogen, chlorides, protein, calcium, phosphorus, phosphatase, total lipids, fatty acids, total cholesterol, cholesterol esters and iodine number) gave results well within normal limits. Biopsy of a specimen taken from the lesion on the outer side of the leg, including the active border, will be described later in the paper.

When the patient was seen in June 1937 in the outpatient department, the erythematous rim around the lesion on the outside of the leg had disappeared, but the infiltration at the periphery was still present. The lesion had enlarged slightly. After this the girl was seen every few months, and each time this lesion had grown, until by January 1938 it had become confluent with the lesion on the back of the leg. In February 1938 the depression extended over the lateral and the posterior aspect of the lower part of the left leg; it had a horizontal diameter of 14 cm. and a vertical diameter of 16 cm. The upper and the lower border felt hard when palpated, because of confluent subcutaneous nodules; this indicated that the lesion was still progressing. These areas were neither red nor tender. The lateral borders of the lesions were smooth. The depression in the thigh had remained inactive. No new lesions had developed. During this time the girl was in good health and as active as other children.

CASE 2.—A 10 year old girl was admitted to the dermatologic department of the Massachusetts General Hospital on Dec. 14, 1937. The family and the past history were irrelevant. In July 1937 there was erythematous pitting nontender swelling of both legs and ankles. In September 1937 the patient was seen at a Boston hospital, and the question of erysipeloid or cellulitis was raised. At that time no nodules were felt. Laboratory examinations done in that hospital, including analysis of the blood, a tuberculin test, culture of material from the throat and a roentgenogram of the legs, showed no abnormality. The sedimentation rate, however, was increased to two and one-half times normal. The swelling and erythema persisted for four weeks and then disappeared. Late in September 1937 both legs showed a patchy purplish discoloration, and beneath this numerous hard nodules appeared and became partly confluent to form irregular areas of induration. The nodules were not elevated above the skin; they were tender to touch, and a drawing pain was experienced in both legs. Gradually the skin became retracted over these areas, so that the distal part of the legs appeared atrophic. New nodules continued to appear. A slight rise in temperature was usually associated with the appearance of these new nodules. Early in December a large subcutaneous node appeared on the outside of the right thigh and after one week developed into a depression 7 cm. in diameter. The most severe attack occurred on December 11 and 12, when the temperature rose to 102.5 F. and nodules appeared on the lower parts of the legs, the soles, the backs of the knees, the inner surface of the right thigh and the extensor surfaces of both arms. These nodules, with the exception of those on the legs, did not exceed the size of a bean and were arranged largely in groups. Pain radiated down the legs and occurred when the knees were extended, and the lumps on the soles caused the patient to limp. On December 14, the day of admission, the pain had almost disappeared. No history of ingestion of drugs could be obtained.

Physical examination showed the girl to be in good health. The distal half of each leg was greatly thinned and the contour irregular, owing to areas of depressed skin, on which there was a discoloration. Palpation showed many

irregularly outlined patches and streaks of induration in the subcutaneous tissue which could not be moved against the skin. The induration extended into the depressions, but the centers of the deeper depressions were usually soft. An area of redness and immovable induration the size of a dime was present on each sole. Several small nodules, mostly the size of a bean and movable under the skin, could be felt at the backs of the knees. One red tender area the size of a 50 cent piece, of indefinite outline and with subcutaneous induration was seen on the inner surface of the right thigh. On the outside of the right thigh was a depressed area 7 cm. in diameter. On the extensor surface of the right arm,

Fig. 2 (case 2).—Right leg in January 1938. The distal part of the leg shows diffuse atrophy of the subcutaneous fat; on the proximal part are three separate deep indentations.

approximately halfway between the elbow and the wrist, four nodules about the size of a pea could be palpated. These were grouped, easily movable under the skin and not tender. The skin over them was unchanged. One small nodule was found on the extensor surface of the lower part of the left arm. Several of the teeth showed cavities.

The temperature was normal during the time of observation in the ward. There was a slight increase in the white blood cell count (11,500) on the day of

admission, but this was subsequently normal. A biopsy specimen was taken from the back of the lower part of the leg, within an indurated area.

Eight days after the patient was admitted to the ward the erythematous indurated lesion on the inner aspect of the right thigh disappeared without leaving any trace. Late in December 1937 the nodules on the soles, the knees and the lower parts of the arms had disappeared. Early in January 1938 three nodules appeared on the extensor surface of the right arm and five nodules on the side and the back of the left thigh. Within one week they were replaced by depressions no larger than a dime, and no induration remained. However, one node on the back of the right thigh continued to be active for a longer time. This lesion became depressed in the center, but the margin remained indurated. In February 1938 this depression had reached the size of a quarter, but the marginal induration had gone. At that time the only active lesions were those on the legs. Here new nodules were still forming at the periphery of the old depressions. However, there was no redness or tenderness, and the child was well and active.

HISTOLOGIC OBSERVATIONS

We believe it appropriate to discuss the sections of both patients together, since the microscopic features were the same.

Subcutaneous Tissue.—The lobules of fat showed wide separation by thick strands of connective tissue, and the fatty tissue contained a diffuse infiltration between and within the fat cells. Two types of cellular exudate could be readily distinguished.

1. In regions in which the fat cells were comparatively well preserved macrophages comprised the greater proportion of infiltrating cells. Interspersed among them in some places were monocytes. The macrophages were large cells with a foamy cytoplasm filled with numerous small vacuoles. Their nuclei were deeply stained, large and irregularly shaped and contained one or more nucleoli and an irregular network of chromatin. The macrophages filled the interstices between the fat cells and by confluence formed giant cells with ten or more nuclei in some places. In many regions the macrophages were within the apparent capsules of the fat cells; they exhibited a pseudoglandular appearance, owing to their arrangement about the concentrically arranged fibrous trabeculae and their epithelial rectangular configuration. Macrophages in many areas actually replaced the fat cells. Occasionally the macrophages appeared to have lost their nuclei and exhibited evidence of necrosis.

2. Focally the fat cells had disappeared and had been replaced by peculiar eosinophilic areolar collagenous tissue within which were scattered lymphocytes, plasma cells, monocytes, fibroblasts and a few polymorphonuclear leukocytes.

The subcutaneous blood vessels appeared much more numerous than usual. Most of them were within the thick strands of connective tissue, but many lay among the fat cells. The blood vessels were dilated; their walls were thickened by perivascular fibrosis, edema and infiltration of

lymphoid cells and occasional macrophages. Within the walls of a few of the veins was apparent separation of the muscle fasciculi by what seemed to be interfascicular edema, giving to the cross sections of the veins a distinctly lamellated appearance. In addition, subendothelial

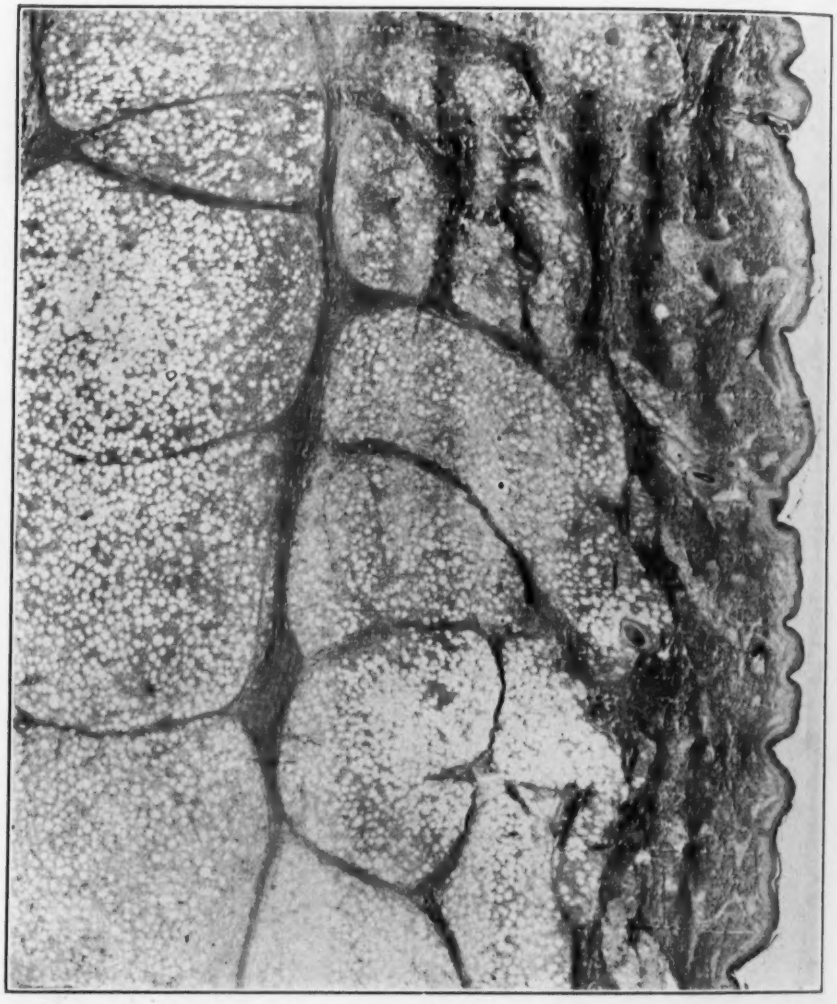


Fig. 3 (case 2).—Low magnification, showing lobulation of the subcutaneous fat by strands of connective tissue and infiltration of the fat. The corium is normal except for vascular changes and infiltration around the sweat glands. Phosphotungstic acid stain.

vacuolation with separation of the endothelial layer from the underlying intima gave a "flame-shaped appearance" to the area between the endothelium and the intima.

Corium.—Within the corium there were moderately increased vasculature, the vessels showing changes similar to those in the subcutaneous tissue, and a scanty perivascular exudate. The sweat glands were sur-

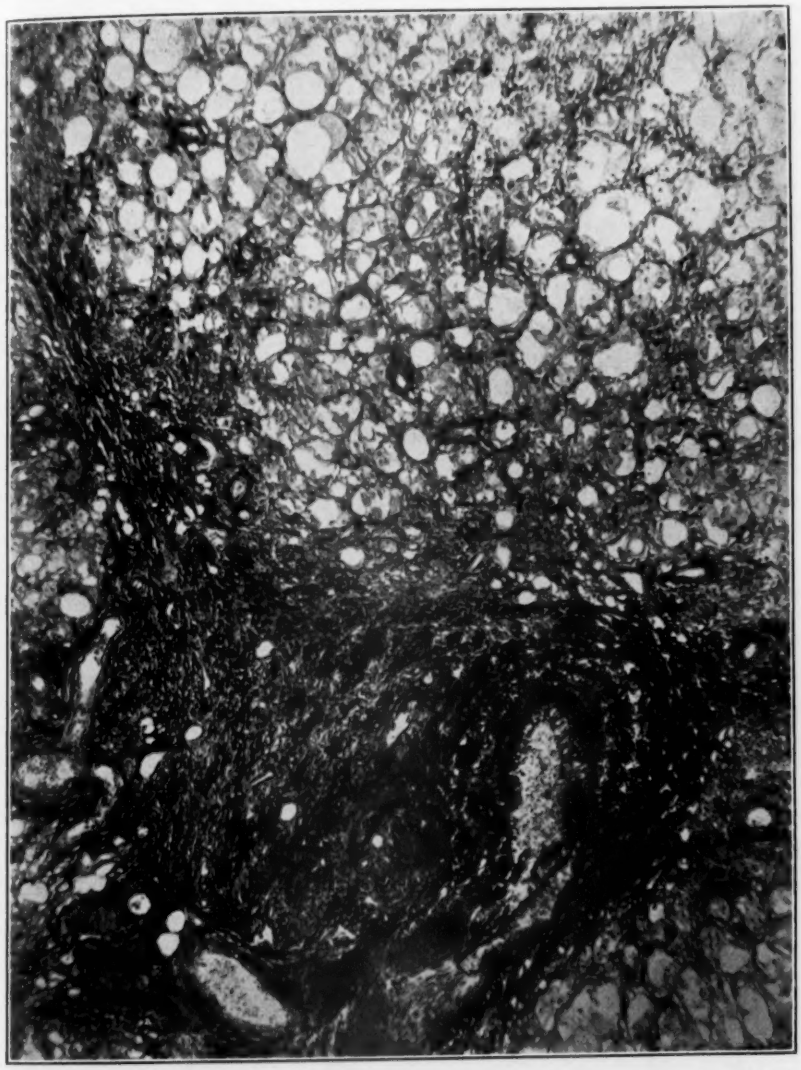


Fig. 4 (case 2).—Section showing three stages. At the top is a large vein the wall of which is thickened and shows intrafascicular and subendothelial edema. The smaller vessels at the right also show lamellation. Aniline blue stain.

rounded by infiltrating macrophages and in some areas lymphocytes. These appeared to separate and compress the glandular ducts. The hair follicles exhibited a similar infiltration.

Fig. 5 (case 1).—High magnification of a vein with marked edema, especially under the endothelium, so that the endothelium appears in several places to be separated from the intima. In most places a connection is maintained by radially arranged fibers with a flame-shaped appearance. Aniline blue stain.

Epithelium.—The epithelium showed no changes within the basal layer and the rete. There was slight hyperkeratosis.

Muscle.—Tissue removed for examination from the first patient showed no pathologic changes.

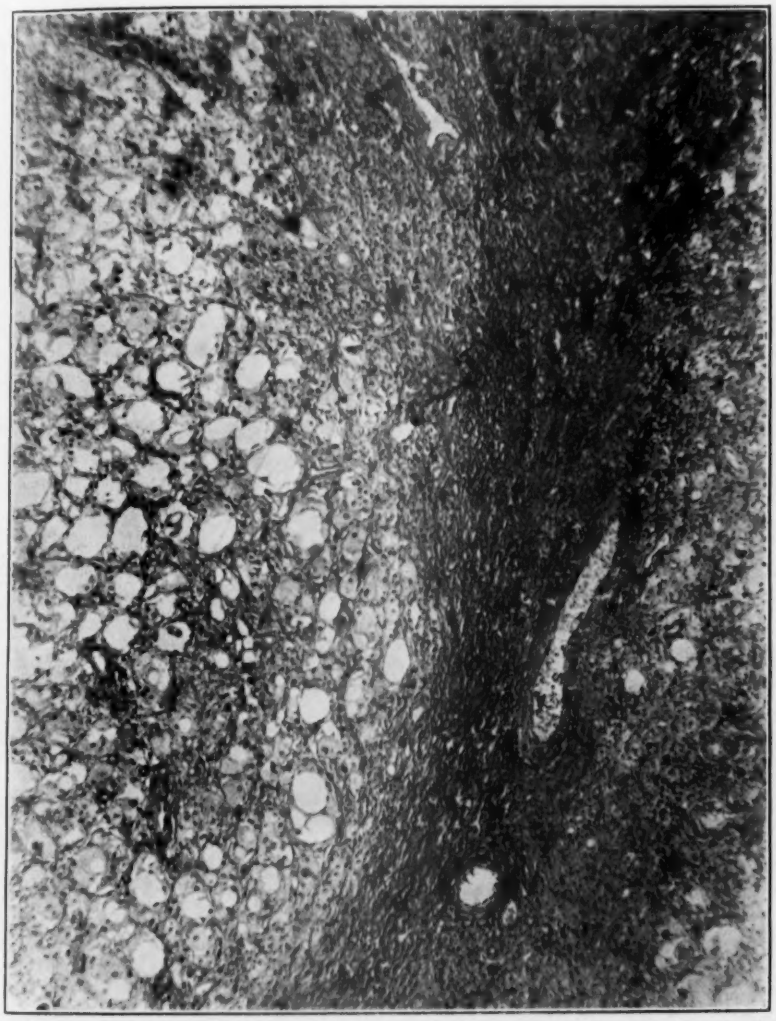


Fig. 6 (case 2).—Section showing three stages of the disease: On the left, the macrophagic infiltration of fat; in the central part, the cellular exudate (lymphocytes, monocytes, plasma cells and fibroblasts) scattered in collagenous tissue, and on the right, fibrotic tissue with few cells. Eosin and methylene blue stain.

Apparently the course of events is as follows: 1. The fat cells are invaded and digested by macrophages. The macrophages, after having digested the fat, become necrotic. 2. Lymphocytes, monocytes and

fibroblasts invade the area in which the macrophages have become necrotic. 3. The inflammatory tissue gradually loses its many nuclei and becomes fibrotic, and contraction ensues. During stages 1 and 2 a nodule is palpable under the skin. During stage 3 depression of the skin develops.

COMMENT

The outstanding features in the 2 cases presented, as compared with the previously reported 13 cases, are:

1. In case 1 fever and malaise apparently never occurred during the development of the three lesions.

2. In case 2 many of the nodules—even the larger ones, which were accompanied with considerable redness and tenderness of the skin—disappeared without leaving any trace. Brill reported this observation in his case.

3. The histologic changes in and around the vessels were striking in both cases, especially the lamellation of the wall and the subendothelial edema, creating a "flame-shaped appearance."

4. In neither case was there a history of ingestion of drugs, which was a factor in 6 of the 13 cases previously reported. The only pathologic finding besides the cutaneous lesions was carious teeth in both cases, which we consider of no etiologic importance.

SUMMARY

Two cases of relapsing febrile nodular nonsuppurative panniculitis have been added to the 13 cases already reported in the literature. A special feature noted in these 2 cases was considerable change in the walls of the blood vessels.

A RELIABLE METHOD OF STAINING SPIROCHAETA PALLIDA IN SMEARS

ARAM A. KRAJIAN
LOS ANGELES

For the identification of Spirochaeta pallida in serous exudates from a suspected superficial lesion the methods available include immediate examination of the material by dark field procedure, the application of various stains to the smear and the india ink method.

A staining method is here described which gives more dependable results than other methods, such as Giemsa's, Fontana's, Ghoregeb's, Gelarie's and others with which I am acquainted.

Experience shows that except in the hands of well trained examiners dark field examinations are not dependable and the proportion of positive findings is much below that actually possible. The biopsy method for demonstrating spirochetes is most satisfactory but entails a certain amount of inconvenience and added cost, which prevents the physician from performing the test on doubtful lesions of skin and mucous membrane. More frequent testing and the consequent finding of syphilis in a higher proportion of cases should result from the availability of a dependable method which can be used conveniently in a well equipped laboratory. The silver stain for smears described here is capable of impregnating within a fifteen minute period even the most resistant spirochetes and offers both convenience and permanence of records.

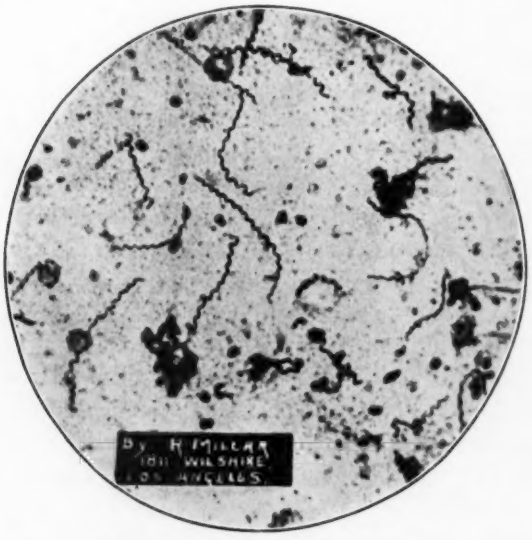
It is, of course, admitted that recognition of the morphologic characteristics of spirochetes on the surface of mucosal lesions may be of less significance than their recognition deep in the tissue of biopsy specimens, but the finding of spirochetes with the morphologic characteristics of S. pallida in smears from a suspicious lesion constitutes at least presumptive evidence of the syphilitic character of the lesion.

TECHNIC

A swab is moistened in alcohol and the lesion roughly rubbed until it bleeds. Several minutes after all the bleeding stops, a clear serous exudate will appear on the abraded surface; from this smears are prepared and dried in air. Each smear is flooded for five minutes with a warm no. 1 solution (uranium nitrate, 1 Gm.; formic acid [85 per cent], 3 cc.; glycerin [chemically pure], 5 cc.; acetone, 10 cc., and alcohol [95 per cent], 10 cc.) washed in distilled water and treated with a weak solution of gum mastic (3 drops of saturated alcoholic solution of

From the Los Angeles County General Hospital.

gum mastic mixed with 7 cc. of 95 per cent alcohol) for two minutes. The gum is poured off and the breath blown over the surface of the smear, which is then rinsed in distilled water. The slide is set on a metal stand or tripod, flooded with a 1 per cent aqueous solution of silver nitrate, heated over a burner until bubbles begin to form (not boiled) and kept at that temperature for three minutes. The silvering process is repeated once, the silver poured off without washing, a thin coat of developing solution applied and the slide left under electric light for two minutes, being warmed gently with a flame. The developing solution consists of hydroquinone, 0.31 Gm.; sodium sulfite, 0.06 Gm.; solution of formaldehyde, 40 per cent neutral, 2.5 cc.; pyridine, 2.5 cc.; saturated solution of gum mastic in 95 per cent alcohol, 2.5 cc., and distilled water, 15.0 cc. The slide is then washed with distilled water, dried in filter paper and examined under



Smear from chancre of the cervix, stained by rapid silver staining method.

an oil immersion lens. For permanent mounts the preparation may be dehydrated with absolute alcohol, blotted, cleared in xylene and mounted in dammar.

Stained smears should be brown.

No. 1 solution is stable and keeps for long periods.

Silver solution should be prepared from a 10 per cent stock solution each time.

Dilute gum mastic should be prepared fresh.

The developing solution keeps well for from two to three weeks in a light room, after which it deteriorates, the gum mastic separating and settling to the bottom of the container. When this occurs, a fresh supply should be prepared.

It is important to use fresh developing solution; otherwise the organisms will fail to stain.

FOLLICULITIS NARIS PERFORANS

REPORT OF A CASE

R. B. PALMER, M.D.
LINCOLN, NEB.

Culver [1] in 1928 reported 3 cases of perforating folliculitis of the naris in which there was extrusion of a vibrissa with its bulbous end pointing toward the cutaneous surface. All 3 patients were men who had consulted him because of the persistence of a pustule on one or the other side of the median line of the cutaneous surface of the tip of the nose. The lesions were of four, five and three weeks' duration, respectively, and had failed to heal despite repeated incision and drainage. In each instance, after removal of a small crust and expression of a droplet of pus, a hair was extracted from the center of the lesion. Following this procedure, healing was prompt. The hairs were typical of those occurring in the nostril, and their bulbous ends were pointing toward the cutaneous surface. They were not like hair from the cutaneous surface, and they were not curled as are so-called "ingrowing hair" (keratosis suprafollicularis).

The explanation which Culver gave for this condition was that owing to an infection in a hair follicle within the nostril the hair became devitalized and separated from its papilla. Through closure of the pustule on the inside of the nostril by serum, crust or dried mucus, the process continued to a greater depth, and external perforation occurred. The course followed from within outward was most likely between the cartilage of the septum and that of the ala nasi, which accounted for the location of the lesion near the median line in all 3 cases. The presence of the loose, dead, infected hair was manifestly the cause of the persistence of the pustule.

Pollitzer [2] expressed the opinion that the condition was rare. Sutton and Sutton [3] stated that it was not so uncommon and that they had observed at least 3 cases. A review of the literature since Culver's report in 1927 reveals no further cases. Among dermatologic text-

1. Culver, G. D.: Perforating Folliculitis Naris, Arch. Dermat. & Syph. **15**:16 (Jan.) 1927.

2. Pollitzer, S., in discussion on Culver.[1]

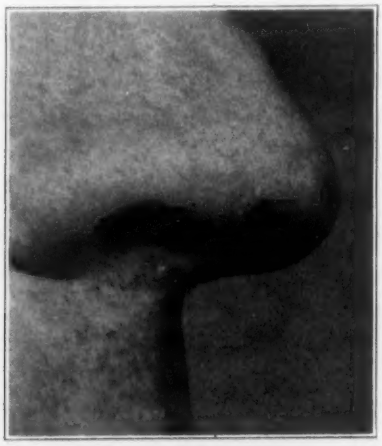
3. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 9, St. Louis, C. V. Mosby Company, 1935, p. 1141.

books available to me, those of Sutton and Sutton [3] and of Ormsby [4] mention the condition. During my three years of dermatologic training and two years of practice, the following case has been the only one of its kind observed:

REPORT OF CASE

T. M., a white man aged 39, was seen on Dec. 9, 1937, because of a small sore on the end of his nose. The lesion was of four or five weeks' duration and was tender and annoying. It had previously been lanced and evacuated several times by the patient, but healing did not occur.

On the right side of the median line of the cutaneous surface of the tip of the nose was a small pustule approximately 3 mm. in diameter, surmounted by a yellowish brown crust and surrounded by an inflammatory areola approximately 2 mm. wide. When the crust was removed a droplet of pus exuded, and after this



Folliculitis naris perforans in a man aged 39.

was sponged away, a hair was seen and extracted. It was fully 1 cm. long, coarse, straight and black, and the bulbous end was outward. Through a lead window 7 mm. in diameter, ½ erythema unit of roentgen rays filtered through 0.5 mm. of aluminum was administered to the lesion. The patient was observed five days later. At this time there was no crust, and the surface of the lesion was healed, although slight redness was still evident.

COMMENT

If this condition is common, explanations for the paucity of reported cases may be: (1) failure of the patient to consult a physician; (2) failure of the physician to recognize the true nature of the condition; (3) failure of the physician to report the case because he considers the condition too insignificant.

I am inclined to believe that the condition is rare.

4. Ormsby, O. S.: Diseases of the Skin, ed. 5, Philadelphia, Lea & Febiger, 1937, p. 1256.

SUMMARY

A case of folliculitis naris perforans is reported. The picture coincides so closely with Culver's description as to leave no doubt of the diagnosis.

1016 Sharp Building.

Clinical Notes

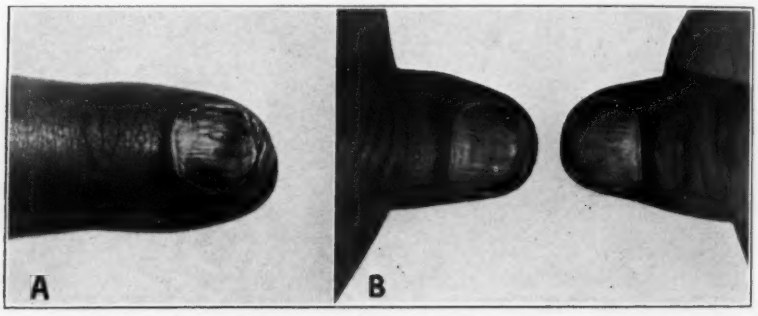
SYPHILITIC ONYCHIA

Report of Case in Which Ungual Changes Helped to Establish the Diagnosis and the Time of Syphilitic Infection

FRANK E. CORMIA, M.D., MONTREAL, CANADA

REPORT OF CASE

Mr. I. J., aged 41 years, in general good health, had an irrelevant past and family history. He was first seen because of an ill defined papular eruption on both palms and soles which was undergoing involution. A few papulosquamous lesions suggestive of psoriasis were seen on the extensor surfaces of the elbows. Imme-



A, syphilitic changes of index finger nail; *B*, multiple Beau lines in early syphilis.

diately distal to the lunula of each thumb nail was a single well marked Beau line. The right index finger was slightly lusterless and showed a few fine whitish longitudinal striations. The examination showed no other abnormality. The patient stated that he had had no recent sexual intercourse, no penile lesion and no generalized eruption.

COMMENT

Late secondary syphilis, psoriasis and atypical lichen planus were considered in the differential diagnosis. The ungual changes were nonspecific and might have occurred in either syphilis or psoriasis. The Wassermann reaction was positive, but active psoriasis with latent syphilis could not be ruled out. Latent syphilis was suggested by his age, by the absence of other early lesions and his statement that he had had no recent sexual intercourse. The location of the Beau lines suggested that a general toxemia, with resultant interference with the function of the nail matrix, had occurred about two months previously. After thorough questioning he recalled that a "few pale spots" had appeared on his abdomen about that time and that a small evanescent papule had been present on the penis about four months ago. He finally stated that he had had a single sexual exposure about five months before.

A diagnosis of atypical late isolated palmar and plantar secondary syphilis was then made, and energetic treatment was begun. Six weeks later the right index finger nail had assumed a striking appearance (fig. *A*), and a second series of Beau lines had appeared on the thumb nails (fig. *B*). The location of these lines on the nails placed their time of onset as simultaneous with that of the isolated palmar and plantar lesions.

The finger nail was the seat of interesting pathologic changes. The nail was slightly lusterless in its distal two thirds and markedly so at its free edge. In the latter area the free margin was irregularly fractured. The entire nail was longitudinally ridged, with some actual fissuring. In three areas the superficial lamellae had partially split off in the form of an eclipse, with resultant dark discolorations. The lunula was large and irregularly diffuse. The nail was slightly hypertrophied and convex in its proximal two thirds, while the terminal third was thinned and concave.

These changes in the index finger nail were considered characteristic of early syphilis. While they might have been classified as onychia craquêle of Fournier, the splitting of the superficial lamellae, in conjunction with the palmar syphilid, made a picture strongly resembling the lesions originally described by Jonathan Hutchinson.[1] The proof of the syphilitic nature of the lesions was demonstrated six weeks later, at which time the newly grown proximal third of the index finger nail was found to be normal in appearance, as a result of the influence of antisyphilitic therapy on the diseased nail matrix.

---

1. Hutchinson, J., cited by Morrow, P.: A System of Genito-Urinary Diseases, Syphilology and Dermatology, New York, D. Appleton and Company, 1893, vol. 2, p. 220.

DERMATITIS DUE TO SHOE LEATHER AND TO SHOE POLISH

LLEWELLYN W. LORD, M.D., AND WILLIAM D. WOLFE, M.D., BALTIMORE

Niles[1] has recently called attention to a clinical entity which is infrequently recognized, namely, sensitivity to shoe leather and resultant dermatitis. This has stimulated us to add 2 cases of an approximately similar condition which have recently been under our observation. We believe that this condition is much commoner than the literature would lead one to suppose and that its true nature is often overlooked.

REPORT OF CASES

CASE 1.—J. E. S., a man aged 22, first consulted one of us (L. W. L.) on July 23, 1928, because of typical dermatomycosis of the feet. He had had the condition on and off for several years, the diagnosis being confirmed when microscopic examination revealed fungi.

At the time of examination the process was practically confined to the dorsa and the webs of all the toes, being more severe on the right foot; there was onychomycosis of both great toes. The condition responded to treatment and on Aug. 15, 1928, the patient was discharged.

He returned on July 10, 1929, when he had an acute attack; this had cleared by August 19.

He presented himself for the third time on April 26, 1930, and this time the condition resisted treatment throughout the summer, clearing eventually on September 30. In the light of our present knowledge of the case, it seems likely that at this time sensitivity to shoe leather first began to develop, and his resistance to treatment may well be attributed to this factor.

He was not seen again until July 22, 1937, when he presented an acute vesicular dermatitis of two weeks' duration. He stated that he had had practically no trouble during the seven years when he had not been seen by us. At this time an acute eczematous eruption involved mainly the dorsal aspect of each great toe and to a lesser degree the distal third of the dorsum of each foot. There were several pyodermic erosions on the great toes, and the process was sharply defined. Between the toes there was little to be seen. Numerous discrete pinhead-sized noninflammatory vesicles were present, being sparse on the hands and most numerous on the dorsal, the medial and the lateral surfaces of the fingers and the medial surfaces of the hands and the thumbs. The diagnosis of dermatomycosis was made clinically, and treatment was started with wet dressings of potassium permanganate and later of modified compound ointment of benzoic acid; a few fractional doses of roentgen rays were given to both hands and feet. The progress of his disease was stormy, with numerous exacerbations and remissions.

The article by Niles aroused our suspicions concerning the role which his shoes might be playing, and when he consulted us on February 10 he was questioned carefully along these lines. He stated that when he wore a certain pair of shoes (fairly old ones), he noticed that his feet seemed to itch more at night after their

1. Niles, H. D.: Dermatitis Due to Shoe Leather, J. A. M. A. **110**:363 (Jan. 29) 1938.

removal. He brought these shoes to us on February 14, and one of them was cut up. Patch tests were made with the cloth lining, the felt lining, the outside leather and the leather of the inner sole. He reacted negatively to the first three substances but gave a definitely positive reaction to the leather of the inner sole. Since that time he has not worn the shoes, and when last seen, on March 11, his feet were free from disease and had been clear since February 25. The eruption on the hands, which had followed the cycle of the eruption on the feet, cleared with the disappearance of the eruption at the site of contact.

CASE 2.—C. H. W., a white man aged 45, consulted us on Sept. 30, 1937, because of an eruption on the dorsa of the feet of fifteen months' duration. During this time he had been treated by several physicians, but had received only temporary relief.

Examination showed an acute vesicular eczematous eruption involving the distal third of the dorsal surface of each foot and the dorsal aspect of all the toes, extending between the right toes. The affected areas were severely excoriated. (At this point we wish to call attention to the comment of Niles regarding excessive itching, which is a feature of contact dermatitis and is much less severe in dermatophytosis.) The patient was treated between September 30 and November 28 with wet dressings of potassium permanganate and later with modified compound ointment of benzoic acid; three fractional doses of roentgen rays were given. He improved rapidly but three relapses occurred.

On November 28 the patient asked whether his shoe polish might be a source of irritation, as each time he polished his shoes (he was accustomed to doing so himself) the feet seemed to become worse. Patch tests were made with his shoe polish ("Two in One") and with several other well known makes; his reaction to his own make was highly positive and to other polishes negative. He removed the polish from his shoes and allowed them to go unpolished for one week, and the process cleared immediately. Since then, by using other shoe polishes he has been able to keep his shoes in condition without any trouble with his skin.

SUMMARY

We present 2 cases in which an eczematous eruption of the feet on casual examination seemed to be dermatomycosis. Further study showed the eruption in 1 case to be due to sensitivity to shoe polish and in the other to sensitivity to shoe leather.

This report is made to show that this disease is undoubtedly much commoner than has heretofore been supposed and that in all cases in which a markedly pruritic eczematous eruption of the feet does not respond promptly to treatment for ringworm investigation should be made for contact dermatitis.

BILATERAL HERPES ZOSTER

HERBERT RATTNER, M.D., CHICAGO

The scarcity of recorded cases of bilateral herpes zoster lends interest to the following case:

REPORT OF CASE

The patient, a man aged 36, a hotel clerk became suddenly ill, with dizziness, fever, vomiting and severe headache, for which he was confined to bed. One week later an eruption appeared in the right supraorbital region, and this was followed in three days by involvement of the left ilioinguinal area. When he entered the Cook County Hospital a few days later, the lesions were typical groups of vesicles on inflamed bases and arranged segmentally, each group stopping at the midline. Throughout the eruptive stage the patient was comfortable; and, as usual in a healthy young man, the disease lasted about two weeks.

COMMENT

Cases in which there is a variation from the usual unilateral arrangement of herpes zoster, particularly the generalized form, are occasionally noted, but not cases in which the eruption is bilateral. In the American literature there have been references to only 20 cases of such involvement. Jacob[1] has recently reported a case in which bilateral herpes zoster was traced to arsenic in the patient's food. In another the patient had been taking solution of potassium arsenite. One instance has been recorded of an infant of 5 months who had bilateral herpes zoster.[2] At a meeting of the New York Dermatological Society in 1915, 2 cases were presented, one by MacKee and Fordyce,[3] in which the condition developed in a man with neurosyphilis, and the other by Howard Fox.[4] In the latter case the bilateral zoster developed one day after the patient was treated with diphtheria antitoxin and vaccinated against smallpox. This was twenty-three years ago, and the late George Henry Fox remarked at the time that he had observed but 2 other cases, and those some thirty years before.

In a few of the recorded cases the eruption involved the buttocks on both sides; in most, however, the eruption appeared on different levels on opposite sides of the body. In the case recorded here the distribution was of the latter type, and because it was an unusual clinical variant of a familiar disease the patient was presented at a meeting of the Chicago Dermatological Society.[5]

Ormsby remarked in discussion that in the cases of bilateral zoster that he had observed the condition differed from the usual infectious type of zoster usually in that there was an obvious causative agent, such as trauma or arsenic.

From the Cook County Hospital.

1. Jacob, F. M.: Bilateral Herpes Zoster Following Acute Arsenic Poisoning, Arch. Dermat. & Syph. **24**:280 (Aug.) 1931.

2. Fox, G. H.: Brit. J. Dermat. **10**:252, 1898.

3. MacKee, G. M., and Fordyce, J. A.: J. Cutan. Dis. **33**:319, 1915.

4. Fox, H.: J. Cutan. Dis. **33**:492, 1915.

5. Rattner, H., and Cornbleet, T.: Bilateral Herpes Zoster, Arch. Dermat. & Syph. **38**:277 (Aug.) 1938.

My patient, however, had been well before his illness, had taken no medicine and so far as he knew had not been exposed to varicella or to herpes zoster. He had worked as a metal plater at one time, when he had been exposed to arsenic, but that had been two years before his attack of herpes zoster. The general physical examination showed no abnormality.

25 East Washington Street.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

CUTANEOUS METASTASES OF MALIGNANT DISEASE. OLIVE GATES, Am. J. Cancer **30**:718 (Aug.) 1937.

The author directs attention to the importance of cutaneous metastasis in the diagnosis of previously unrecognized malignant growths. Cutaneous metastases are sometimes observable months or years before death but usually do not appear until there has been extensive internal metastasis. Of a series of 2,300 autopsies in cases of malignant disease there were metastases to the skin in 2.7 per cent. These were almost equally divided among epithelial and mesenchymal lesions. Half of the epithelial malignant growths originated in mammary cancer. Dissemination was apparently more frequently lymphatic than hematogenous, but there did not appear to be types of tumor with a predilection for cutaneous metastasis, which was most frequent in cases in which there were the most extensive internal metastases.

PRODUCTION OF EPITHELIAL TUMORS BY IRRADIATION OF A PRECANCEROUS SKIN LESION. J. C. MATTRAM, Am. J. Cancer **30**:746 (Aug.) 1937.

Experimentally produced benign warts in tarred mice were subjected to gamma rays of radium. It was observed that where irradiation was insufficient to destroy the epidermis a greater number of epithelial tumors appeared than would apparently have developed without irradiation. Conversely, where destructive doses were applied to the epithelium, epithelial tumors were destroyed or their growth inhibited. The author infers from these experiments that precancerous lesions may be stimulated to more active growth by small doses of radiation.

FOERSTER, Milwaukee.

HUMAN AUTONOMIC PHARMACOLOGY: VI. GENERAL AND LOCAL SWEATING PRODUCED BY ACETYL-BETA-METHYL CHOLINE CHLORIDE (MECHOLYL). ABRAHAM MYERSON, JULIUS LOMAN and MAX RINKEL, Am. J. M. Sc. **194**:75 (July) 1937.

Subcutaneous injection of mecholyl results in drenching perspiration, increasing in alkalinity as the reaction goes on. This action of mecholyl is inhibited by atropine and enhanced by prostigmine and physostigmine. A local sweating effect was noted after intradermal injection of mecholyl.

The authors comment on seasonal variations in the response to these experiments.

STUDIES IN SYPHILITIC CARDIOVASCULAR DISEASE: I. UNCOMPLICATED SYPHILITIC AORTITIS; AN ASYMPTOMATIC CONDITION. ROBERT WILSON JR., Am. J. M. Sc. **194**:178 (Aug.) 1937.

In a series of 1,619 autopsies, Wilson records an incidence of 13 per cent of syphilitic involvement of the aorta. Analysis of the presenting symptoms indicates that in practically every case in which cardiac or respiratory symptoms were present they have been shown to be due to some factor other than uncomplicated syphilitic aortitis. It is concluded that uncomplicated syphilitic aortitis is an asymptomatic condition and that no symptoms are reliable as criteria for the making of an early diagnosis.

TUBERCULIN SKIN SENSITIVITY IN CHRONIC TUBERCULOSIS IN THE COURSE OF HOSPITAL TREATMENT: MEASUREMENT BY STANDARD TUBERCULIN (PURIFIED PROTEIN DERIVATIVE). MARIAN G. HAYES, J. R. PASTOR, L. R. GAETAN, RICHARD CORY and E. R. LONG, Am. J. M. Sc. **194**:220 (Aug.) 1937.

Fluctuations in the intensity of the cutaneous reaction to tuberculin were studied by monthly tests in 116 ward patients with chronic pulmonary tuberculosis. Of the 67 patients given injections at 5 or more monthly intervals, more than half maintained approximately the same level of sensitiveness, as did 12 of 20 who were followed for approximately a year. The fluctuations in the remainder were inconstant, but certain consistent trends were observed. While, as is already well known, patients in whom the condition took an unfavorable course tended to lose their sensitiveness to tuberculin as the end approached, a definite continuing depression of sensitivity was observed in patients with chronic tuberculosis of long duration but a somewhat favorable course. On the other hand, a transient or prolonged increase in sensitiveness occurred in numerous patients in association with clinical improvement.

LYNCH, St. Paul.

CLINICAL EXCRETION OF BISMUTH: II. THE URINARY EXCRETION OF BISMUTH AFTER CLINICAL INTRAMUSCULAR INJECTIONS OF SODIUM IODOBISMUTHITE (SODIUM BISMUTH IODIDE, IODOBISMITOL) AND SODIUM BISMUTH THIOGLYCOLLATE (THIOBISMOL). T. SOLLMANN, H. N. COLE, K. HENDERSON, G. W. BINKLEY, W. H. CONNOR and M. SULLIVAN, Am. J. Syph., Gonor. & Ven. Dis. **21**:480 (Sept.) 1937.

The urinary excretion of iodobismitol after intramuscular injections resembles closely that following administration of the watery solutions of sodium bismuth citrate or the alkali bismuth tartrates, with some difference of degree, in that the excretion of iodobismitol is distinctly more sustained, so that two injections a week suffice to maintain the same progressively rising level of excretion as three injections of citrate and tartrate. The iodobismitol, therefore, constitutes a transition to the oil suspension of the tartrate and the oil solutions.

Thio-bismol stands at the other extreme of the watery solution, in that its intensive urinary excretion is of short duration, the peak excretion being usually confined to the day of injection, with a low level on the succeeding day. There is, consequently, little or no cumulation in the excretion. Thio-bismol is especially suited for rapidly attaining relatively high concentrations for brief periods, if the injections are given every other day.

CLINICAL EXCRETION OF BISMUTH: III. FECAL AND TOTAL EXCRETION. T. SOLLMANN, H. N. COLE, K. HENDERSON, G. W. BINKLEY, W. H. CONNOR and M. SULLIVAN, Am. J. Syph., Gonor. & Ven. Dis. **21**:492 (Sept.) 1937.

When bismuth has been administered clinically, the ratio of fecal to total excretion of bismuth varies rather widely for different patients. The medians show that it is relatively low for the oil solutions; then follow oil suspensions, iodobismitol with saligenin and finally thio-bismol.

The excretionary efficiency of the preparations studied, judged by the total (urinary and fecal) excretion compared with the amount injected, is highest for iodobismitol with saligenin; second comes thio-bismol; then, in descending order, biliposol, tartrate in oil, bismo-cymol, tartrate in water, citrate in water and ethylene glycol and salicylate in oil.

The total quantity of bismuth retained with the clinical dosage is largest with salicylate in oil, probably owing to the limited absorption from the injection deposits. Then in descending order of retained bismuth come the oil solutions, thio-bismol, tartrate in oil, tartrate and citrate in water and iodobismitol with saligenin. The absorptions of these are so good that the retention must be due chiefly to deposition in the tissues, which probably is not desirable yet which clinically has no serious import.

CLINICAL EXCRETION OF BISMUTH: IV. THE LATE EXCRETION OF BISMUTH AFTER CESSATION OF TREATMENT. T. SOLLMANN, H. N. COLE, K. HENDERSON, G. W. BINKLEY, W. H. CONNOR and M. SULLIVAN, Am. J. Syph., Gonor. & Ven. Dis. **21**:506 (Sept.) 1937.

The urinary excretion of bismuth after routine clinical courses may show wide individual variations which may be greater than the differences due to dosage. The medians, however, show that the higher doses produce higher excretion. The daily excretion after cessation of injections descends logarithmically, i. e., as parabolic curves. These are steeper for the higher levels of excretion and become nearly horizontal when the daily excretion falls below 1 mg. or 0.5 mg.; this level continues practically indefinitely.

Presumably this continued excretion at the lower levels represents remobilized bismuth which had been deposited in the organs, while the excretion at the higher levels with a steeper fall reflects continued absorption from the depots of injection. The slope is steepest for the more rapidly absorbed iodobismitol with saligenin and biliposol and least steep for the more slowly absorbed oil suspensions of salicylate and tartrate. The late fecal excretion of bismuth shows a similar relation to dose. The quantity averages generally less than 1 mg. per day at any time.

REUTER, Milwaukee.

SCLERODERMA WITH CALCINOSIS. C. P. HOWARD, Canad. M. A. J. **37**:124 (Aug.) 1937.

In 2 cases scleroderma was associated with deposition of calcium in nodes. In 1, destructive arthritis was also present. Howard reviewed the literature pertaining to this association. The differential diagnosis embraces a consideration of (1) uratic tophi of true gout, (2) calcareous concretions without scleroderma, (3) cutaneous concretions of Raynaud's disease, (4) acrodermatitis atrophicans and (5) myositis ossificans. Suggested therapy includes good hygiene, a ketogenic diet, glandular (thyroid, ovarian, hypophysial and pluriglandular) extracts, surgical removal, if desired, of certain of the internal glands, periarterial sympathectomy and various symptomatic measures.

CONTACT ECZEMA FROM DYED CLOTHING. J. F. BURGESS, Canad. M. A. J. **37**:237 (Sept.) 1937.

Burgess reports the cases of 6 women who presented eczematous eruptions. In all cases a new dress or one newly dyed had been worn, and the eruption was on the skin covered by and in contact with the suspected garment. A patch test with a sample of the dress gave a positive result in each instance, and cure followed discard of the dress.

VALUE OF MAPHARSEN IN TREATMENT OF CONGENITAL SYPHILIS. E. A. MORGAN, Canad. M. A. J. **38**:53 (Jan.) 1938.

Morgan treated 40 patients who had congenital syphilis with mapharsen for sixteen months. In all, 935 intravenous injections were given, 133 attended by some reaction. There was only one immediate reaction and one attack of jaundice. The other reactions occurred about one and a half hours after the injection and consisted of nausea, vomiting and slight headache, lasting one or two hours. Care in adjusting the dose of the drug cuts down the number of reactions. The drug is favorably considered by Morgan as an agent in effecting a serologic cure.

DERMATITIS CAUSED BY DICTAMNUS ALBUS (GAS PLANT). C. L. CUMMER and R. DEXTER, J. A. M. A. **109**:495 (Aug. 14) 1937.

Cummer and Dexter report the case of a man in whom a dermatitis of the forearms was found to be caused by sensitivity to Dictamnus albus. Contact with

the plant did not cause a reaction unless the site was subsequently exposed to ultraviolet rays. Residual pigmentation in the affected sites persisted for weeks or months and in this way resembled berlock dermatitis.

GONADOTROPIC SUBSTANCE IN TREATMENT OF ACNE. G. E. WILLIAMS and R. NOMLAND, J. A. M. A. **109**:564 (Aug. 21) 1937.

In order to determine the effectiveness of gonadotropic substance from the urine of pregnant women in the treatment of acne, Williams and Nomland administered the product by intramuscular injection to 20 patients. Nineteen patients with acne were kept on a topical, hygienic and dietary regimen similar to that of the treated group but were given injections of sterile water instead of the gonadotropic substance. Eighty-five per cent of those given the gonadotropic substance showed moderate to marked improvement, while 78 per cent of the control group given sterile water were similarly improved. Williams and Nomland concluded that this improvement resulted from the other remedies given and that a deficiency of the gonadotropic hormone is not an important etiologic factor in acne.

LEWIS, New York.

VITAMIN DEFICIENCY DISEASES: THEIR DIAGNOSIS AND TREATMENT. D. L. WILBUR, M. Clin. North America **12**:737 (May) 1937.

While the gross manifestations of vitamin deficiency are now easily recognized, clinical and experimental evidence of the existence of states of partial deficiency, elusive in their symptoms, is gradually accumulating. Two factors are most concerned in the production of these deficiency states in this country, where the foods consumed are rarely inadequate in quantity. Those are destruction of vitamins in processing and changes in the gastrointestinal tract which lead to inadequate absorption even though the diet contains a sufficient supply of essential substances.

"Vitamin A is probably a catalyst in its chemical action, and physiologically it is essential for the maintenance of the integrity and normal state of all epithelial tissues." In deficiency, these tissues lose their normal appearance, and thickening or keratinization, followed by secondary infection, results. To these epithelial changes may be attributed the ocular symptoms and cutaneous lesions occurring in vitamin A deficiency. Contrary to popular opinion, vitamin A is not an anti-infective agent.

Vitamin B, while apparently a catalyst chemically, is physiologically an essential factor in the metabolism of carbohydrates, probably having some part in the oxidation of lactic acid and pyruvic acid. Deficiency is manifest clinically by such nervous symptoms as peripheral neuritis, paresthesias of the extremities and tenderness of the muscles, with weakness or paralysis. Certain intestinal disturbances, especially anorexia, may result from dietary deficiency of this vitamin. Therapeutically, crystalline B_1 does not seem to represent all the factors of the vitamin. Brewers' yeast, however, apparently contains an essential substance not present in crystalline and concentrated forms.

Vitamin C is a powerful reducing substance and physiologically is essential in the formation and the maintenance in a normal state of intercellular substance, particularly of the blood vessels, tooth-forming organs and connective tissue.

Vitamin D plays an essential part in the metabolism of calcium and phosphorus. Hence, its use in the prevention and cure of rickets, in the treatment of certain bone diseases and tetany and in the promotion of normal dentition is on a sound physiologic basis.

Vitamin B_2 or G is the heat-stable or antidermatitic factor of the original water-soluble vitamin B. It is apparently composed of two fractions, neither one of which alone possesses the growth-promoting action which together they manifest. Singly or together, the two factors are essential for normal functioning of the skin, the nervous system and the gastrointestinal tract. The richest sources of vitamin G are fresh leafy vegetables, cream, milk, eggs, beef, potatoes, citrous fruits and especially yeast extracts and liver extract.

EUGENE SMITH, Ogden, Utah. [AM. J. DIS. CHILD.]

VARICELLA GANGRENOSA DUE TO STREPTOCOCCUS PYOGENES. H. S. BANKS and J. E. MCCARTNEY, Lancet **2**:311 (Aug. 7) 1937.

A rapidly fatal massive gangrene of the skin, complicating the early eruptive stage of chickenpox, is described. The patient had concurrent severe tonsillitis. During life cultures of material from the nose and the throat showed staphylococci and hemolytic streptococci, and cultures of material from the gangrenous areas, Staphylococcus aureus. Postmortem cultures of the cardiac blood and of excised pieces of various lesions showed an almost pure growth of hemolytic streptococci. It is assumed that the tonsillitis was the source of the streptococcic infection.

LANGMANN, New York. [AM. J. DIS. CHILD.]

ANNULAR ERYTHEMA AND STREPTOCOCCEMIA IN THE COURSE OF BOUILLAUD'S DISEASE. R. DEBRÉ, M. LAMY and M. L. JAMMET, Arch. de méd. d. enf. **40**:357 (June) 1937.

Six cases of annular and marginated erythema in children suffering from acute articular rheumatism are reported. Cultures of the blood of 2 patients revealed the presence of Streptococcus viridans and demonstrated the relation between Bouillaud's disease and malignant endocarditis of the retarded type.

Cutaneous eruptions in the course of acute rheumatic disease of childhood have been recognized since Rayer, in 1833, recorded his classic observations. They may occur early in the invasion, preceding by several days the articular or cardiac symptoms. The parts involved include the thorax, the abdomen, the loins and, less frequently, the neck and the limbs; the face and the mucous membranes are always spared. The eruption is usually light and may easily be overlooked; it appears, spreads and disappears in a few hours, so that the topography of the rash is continually changing. The color varies from lilac to copper and disappears under pressure; as the rash extends, the center of the pattern becomes pale, while the periphery shows a more intense discoloration, giving the typical ringlike appearance described by dermatologists of the Viennese school. There is neither itching nor desquamation. The only disorders which might confuse one in diagnosis are the so-called fifth disease and infectious erythema.

AMESSE, Denver. [AM. J. DIS. CHILD.]

RESULTS OF THE TREATMENT OF ECZEMA IN INFANTS WITH BCG. P. WORINGER, Bull. Soc. de pédiat. de Paris **34**:442, 1936.

The statement is made that infantile eczema improves for a short time after acute infection but often remains cured after chronic infection. Seventy-seven infants with eczema were given BCG subcutaneously; at first a dose of 1 cc. was used, and later the dose was increased to 5 cc. Fifty-five were cured of eczema within four weeks; some improved slowly, and 11 continued to have eczema for more than two and a half months. In the last group the treatment was considered to have failed. It is felt that if BCG is given at an early age the results are better than if it is given later; the results at from 2 to 5 months of age were all good. Doses of from 4 to 5 cc. gave better results than smaller ones. Local treatment of the skin was employed, and it was found that coal tar ointment was the most efficacious medicament.

ERYTHEMA NODOSUM AS EVIDENCE OF INCREASED ALLERGY TO TUBERCULIN: ITS APPEARANCE FOLLOWING TUBERCULIN REACTIONS. J. J. BINDSCHEDLER, Bull. Soc. de pédiat. de Paris **34**:545, 1936.

This is a report of 4 observations of erythema nodosum following the tuberculin test in children. The possibility that the tuberculin test increases hypersensitiveness to tuberculin just enough to bring out erythema nodosum as an allergic manifestation is discussed.

BENJAMIN, Montreal, Canada. [AM. J. DIS. CHILD.]

CONGENITAL ABSENCE OF SKIN AREAS. P. TRILLAT and P. CORNUT, Nourrisson **25**:117 (March) 1937.

The infant whose condition is described was born at term and developed normally except that its right forearm was undersized, owing to the smallness of the bones and muscles. On the extensor surface of this forearm were two areas devoid of skin, one measuring 3 by 2 cm. and the other 3 by 1 cm. At the end of ten days the areas had cicatrized without special treatment.

The Wassermann reactions of the mother's blood and of blood from the umbilical cord were negative. McCLELLAND, Cleveland. [AM. J. DIS. CHILD.]

TRAUMATIC ALOPECIA. P. L. BALINA, Rev. argent. de dermat. **21**:31, 1937.

Balina reports a case of alopecia of the temporal and the occipital region, due to trauma from mechanical curlers. This type of alopecia has been described by Sabouraud under the name *alopecia liminaire,* and its cause has puzzled observers for some time. Balina has proved that the hair is pulled by the curlers so that many hairs break off, while others are simply pulled out. Braiding the hair tightly may have the same effect. Balina calls attention to the presence of a number of thinned and "exclamation point" hairs in these areas of alopecia.

ATYPICAL MYXEDEMA COINCIDENT WITH EXOPHTHALMIC GOITER. LUIS E. PIERINI, Rev. argent. de dermat. **21**:43, 1937.

The patient reported on by Pierini had suffered from exophthalmic goiter; the thyroid gland had been partially removed, and high voltage roentgen therapy had been applied. The basal metabolic rate, which had been +39 per cent, was reduced to normal. Seven months after the operation the patient presented a pruriginous and erythematous plaque on the left ankle, with prominent hair follicles and hypertrichosis of the legs. Later the condition spread to the rest of that leg and to the opposite leg. The affected skin appeared thickened, dark red or yellowish, raised over the level of the normal skin and covered with perifollicular lichenoid papules. In some places a few smaller deep red lesions were observed, which Pierini considered as the initial changes. The patient presented other symptoms of hyperthyroidism, and the basal metabolic rate was +14 per cent. The pharmacodynamic tests all gave positive results indicative of hyperthyroidism. Histologic examination showed deposits of mucoid substance in the corium. No improvement was obtained with thyroxin treatment, and the patient grew gradually worse, the basal metabolic rate rising to +25 per cent. PARDO-CASTELLO, Habana, Cuba.

NONSPECIFIC THERAPY IN SYPHILIS. MARGOT VON HECHT-ELEDA and GUSTAV RIEHL, Arch. f. Dermat. u. Syph. **176**:8, 1937.

Thirty-three patients with latent seropositive syphilis, 4 with early latent syphilis and 3 with prenatal syphilis were given twelve injections (from 5 to 10 cc. at intervals of three or four days) of their own blood, which had been given ultraviolet radiation from a quartz mercury vapor lamp for from one to three minutes. The serologic reaction became negative in 27 per cent of cases, was improved in 25 per cent and remained unchanged in 48 per cent.

Control injections of their own nonirradiated blood showed only 1 reversal of the reaction to negative in 10 patients. In the others the serologic reactions remained unchanged.

STREPTOCOCCIC DERMATOSES. E. BIZZOZERO and R. LEONE, Arch. f. Dermat. u. Syph. **176**:16, 1937.

The authors exposed deep layers of the epidermis and inoculated the lesions with streptococci, with mixtures of streptococci and staphylococci 4:1 and 1:4 and with staphylococci. Virulent streptococci produced lesions of ecthyma in

practically 100 per cent of cases. The lesions following inoculation of streptococci were more inflammatory, and those following the other three inoculations were identical. Addition of staphylococci to the lesions of streptococcic ecthyma caused no alteration in the course.

Inoculation into lesions of chronic inflammatory diseases (neurodermatitis, psoriasis, lupus erythematosus and subacute eczema) resulted in abortive lesions. Repeated inoculation of streptococci into exudative eczematoid lesions produced no impetiginous eruption. Virulent organisms were cultured from dried crusts of healing lesions of streptococcic origin. Inoculation into healed lesions produced earlier reaction but more transient lesions than inoculation in the normal skin.

The authors conclude that there is variation in individual and regional predisposition to infection with streptococci and that the involved skin is allergic after healing of the lesions.

BECKER, Chicago.

THE FATE OF PATIENTS WITH MYCOSIS FUNGOIDES. A. JORDAN and W. ARESCHEWA, Dermat. Ztschr. **74**:126 (Oct.) 1936.

The authors present a statistical study of 136 cases of mycosis fungoides taken from the literature and some cases of their own. The study includes all reported cases in which sufficient data were published to warrant their inclusion. Of these cases, 68 were followed for from one to five years, 38 for from six to ten years, 8 for from eleven to fifteen years, 5 for from sixteen to twenty years, 1 for twenty-four years and 1 for thirty years. In 15 cases the time of observation was not stated. Only 38 cases were followed to the fatal termination. Of these, death came as a result of cachexia in 10, probably of damage from roentgen rays in 10, of metastases to the internal organs in 4, of complications occurring in the lungs, the heart, the brain or the endocrine glands in 5, of intercurrent disease in 1 and of an unstated cause in 8. Roentgen irradiation is the most helpful therapeutic measure but must be limited on account of the danger of damage from the rays.

THE LOSS OF HAIR AS A SYMPTOM OF MASCULINIZATION IN A WOMAN. HUGO FASAL, Dermat. Ztschr. **74**:249 (Dec.) 1936.

Fasal reports the case of a woman 40 years of age in whom a masculine type of baldness developed. There was alopecia of the temporal portion of the scalp and of the vertex, while the central anterior area remained covered with hair. At the age of 27 years she had had some ovarian disease, and shortly afterward an increase of hair on the body was noted. There was no evidence of adrenal or ovarian tumor. A brief review and discussion are given of similar cases previously reported.

TAUSSIG, San Francisco.

TREATMENT OF CUTANEOUS CANCER WITH CONCENTRATED FRACTIONAL NEAR IRRADIATION, ACCORDING TO THE METHOD OF CHAOUL. K. SO and T. KOBORI, Jap. J. Dermat. & Urol. **42**:184 (June) 1937.

The authors used roentgen rays in 5 cases of cutaneous cancer, according to the method of Chaoul, using 60 kilovolts, 4 milliamperes, a 0.3 mm. copper filter, a focal skin distance of 3 cm. and a daily dose of 400 roentgens (66.6 r per minute). They came to the conclusion that this method of Chaoul is superior even to the use of radium in the treatment of cutaneous cancer.

ECZEMA AND SERUM LIPASE. T. OZAKI, Jap. J. Dermat. & Urol. **42**:256 (Nov.) 1937.

The author investigated the activity of serum lipase after the production of experimental dermatitis in rabbits. He found that during the acute and the early subacute stage the activity of serum lipase was considerably diminished, in the subacute end stage increased and in the stage of healing normal. Although this

change in the activity of serum lipase does not parallel the change in cholesterol, it is in the same direction as that of total lipids and that of phosphatides. In the acute and the subacute stage of the dermatitis half of the rabbits showed loss in weight and the other half no loss or even an increase. According to the author, the change in the activity of serum lipase in experimental dermatitis is a secondary manifestation accompanying the organic and functional disturbances of the internal organs.

RED PATHOGENIC YEAST FUNGI. R. TAKASU, Jap. J. Dermat. & Urol. **42**:258 (Nov.) 1937.

The author has made mycologic and biologic studies and experiments with animals with red yeast fungi which he cultured from sputum, from urine and from pathologic lesions in man.

By his experiments the author believes he has found among the yeast fungi which produce red pigment many different species, of which some are pathogenic for men and animals.

CLINICAL AND HISTOLOGIC STUDIES ON SO-CALLED ESTHIOMENE. Z. FUJITA, Jap. J. Dermat. & Urol. **42**:261 (Nov.) 1937.

The author studied 8 cases of the symptom complex which was described by P. C. Huguier (*Mém. Acad. de méd.* **14**:501, 1849) as "esthiomene of the vulva and the perineum." He made the following observations: Most of the patients were prostitutes, and the rest were infected by husbands who had buboes. The Frei reaction was strongly positive in all cases. From the different pathologic tissues, such as the elephantiasic external genitals, the chronic ulcer, the wall of the fistula, the stricture and the polypous hyperplastic area in the rectum, an effective Frei antigen could be produced. This symptom complex is not caused by syphilis, chancroid, gonorrhea or tuberculosis. Esthiomene is a manifestation of infection with the virus of lymphogranuloma venereum.

Histologic examination was made of a polypous tumor, the elephantiasic tissue, the ulcers of the rectum and vulva, the stricture of the rectum and the fistulas. All of them showed chronic or subacute inflammatory granulomatous lymphoma. There was marked organization of connective tissue. (The process starts with an exudative infiltration consisting of lymphocytes, histiocytes, etc., and is gradually surrounded by granulomatous tissue, which becomes organized.) The formation of granulation tissue from the cellular infiltration resembles markedly that of the bubo or of the primary lesion of lymphogranuloma venereum. The author believes that the special anatomic conditions of the lymphatic system in women cause the involvement of the pelvic lymph glands to be marked; lymph stasis results, and the purulent chronic inflammatory changes are thereby produced in the rectum and the vulva.

The author believes that the syndrome of esthiomene is not a secondary result of lymphogranuloma venereum, but a special form of the disease.

RESULTS OF EXPERIMENTAL INVESTIGATION ON CUTANEOUS STORAGE OF DYES. S. OHMORI, Jap. J. Dermat. & Urol. **42**:262 (Nov.) 1937.

The author investigated the storage of dyes in artificially produced wheals in rabbits. He found, among twenty dyes tested, three acid-vital dyes belonging to the diazo group, namely, congo red, trypan blue and trypan red, to be stored in the greatest amount in the wheal. Of these three dyes, congo red was most successfully investigated because it produces even discoloration of the wheal and no discoloration of the surrounding skin, and is practically nontoxic. The author explains the storage of congo red in the urticarial wheal by the permeability of the capillaries and the diffusion of the dye through the tissue. The more hypertonic the wheal, the larger the amounts of congo red diffused. In rabbits in which alkalosis or acidosis was produced, the storage of dye was accelerated

and the intensity of color of the wheal produced by histamine or by morphine was increased. By injection of epinephrine or pilocarpine the storing of the dye was inhibited.

PEMPHIGUS LEPROSUS. E. YAMASAKI, Jap. J. Dermat. & Urol. **42**:269 (Nov.) 1937.

The author investigated 19 cases of bullous leprosy, and he concludes that bullae occurring in the early stage of leprosy are due to trophic (because of neural involvement) and to circulatory (due to infiltration of the vessel walls) disturbances. Stasis and marked edema of the cutis and the germinal cell layer lead to the *alteration cavitaire* of Leloir and finally to bullae. External trauma may be an exciting factor. The broken bullae become secondarily infected and ulcerated.

BLOOM, New York.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

LOUIS CHARGIN, M.D., *Chairman*

Jan. 4, 1938

HARRY C. SAUNDERS, M.D., *Secretary*

Sarcoid of Boeck, Lichen Scrofulosorum and Papulonecrotic Tuberculid.
Presented by DR. G. F. MACHACEK.

E. T., a woman aged 57, was previously presented by Dr. A. Benson Cannon before the New York Dermatological Society on Dec. 21, 1937 (ARCH. DERMAT. & SYPH. **38**:91 [July] 1938).

Histologic examination of a specimen from the lesion on the chin showed a tuberculoid-sarcoid structure. Two biopsy specimens from the follicular papular lesions five years ago showed lichen spinulosus. Cultures of material taken recently from the tongue and the nails showed Monilia. Roentgen examination showed no changes in the bone and only heavy bronchovascular markings in the lungs. The Wassermann reaction was negative. Injections of a bismuth preparation did not cause improvement in the eruption.

DISCUSSION

DR. MARION B. SULZBERGER: This case is presented with a great many diagnoses for a single eruption. I see no lesions typical of sarcoid. Even the lesion on the chin does not seem characteristic of sarcoid. The color and the surface of the lesion are not identical with those usual for sarcoid. Moreover, the patient has parakeratotic lesions with some exudation in one area on the leg. Some denudation and a shiny reddened moist surface are apparent. In addition to the other diagnoses offered, I should like to venture the possible diagnosis of the Senear-Usher type of pemphigus with lesions resembling psoriasis and seborrheic eczema.

DR. ISADORE ROSEN: I noted some of the eczematous manifestations mentioned by Dr. Sulzberger and I think they are due to the removal of scales by the various physicians examining the patient. There are small and large lesions with scales which closely resemble the micaceous scales of psoriasis. The whole picture would readily fit in with that disease. If microscopic examination of the large lesions of the thigh shows sarcoid, the clinical diagnosis will have to be altered.

DR. LOUIS TULIPAN: In addition to the lesions Dr. Rosen mentioned, I found two scaly patches on the scalp which the patient did not know she had and which were typical of psoriasis, and there is dystrophy of one of the nails. It is broken off and seems to be brittle. I agree with Dr. Rosen. The whole picture seems to be that of psoriasis.

DR. OSCAR L. LEVIN: This case is most unusual and interesting. In addition to the manifestations already mentioned, the patient presents lesions which suggest parapsoriasis, those on the lower extremities showing loosely adherent scales and a superficial inflammation. I do not believe that the eruption bears any relation, as suggested by Dr. Sulzberger, to pemphigus. There are small papular follicular lesions, probably manifestations of a generalized toxic reaction, and on the right cheek is a distinctly brownish yellow lesion which I believe to be a manifestation of tuberculosis, probably a sarcoid. The lesion on the left cheek, however, suggests

lupus erythematosus. It is my opinion that the patient presents various cutaneous manifestations due to a tuberculous infection probably resulting from old disease of the kidney.

DR. J. GARDNER HOPKINS: I think the fact that an eruption that shows a tuberculoid structure histologically can be mistaken by so many able dermatologists for psoriasis is an interesting example of the difficulty of clinical diagnosis.

DR. FRANK C. COMBES: I agree with the diagnosis as presented. I do not know how to make a diagnosis of sarcoid clinically. I think that problem has been well explained tonight. As for lichen scrofulosorum, only one lesion, on the left shoulder, is typical of the condition. I do not think that was mentioned in the history. The lesions on the legs do not remotely resemble lichen scrofulosorum in their configuration, their location or their other clinical characteristics. However, if histologic examination shows a tuberculoid structure, I see no reason why this patient could not have lesions which conform to our usual conception of sarcoid and possibly papulonecrotic tuberculid and lichen scrofulosorum.

DR. GEORGE C. ANDREWS: I think that the members who looked at this patient quickly and superficially and got the impression of psoriasis did not read the history and did not know that Monilia had been observed on microscopic examination. Some of the lesions are undoubtedly moniliasis. The lesion of the left little finger nail and some of the psoriasiform scaly patches are accounted for by that diagnosis. The patient has perlèche at the corners of the mouth.

DR. G. F. MACHACEK: This case had my colleagues and me puzzled for several years, just as it has puzzled the members this evening. Originally I knew, of course, the tuberculous background of this patient. It was established pathologically and bacteriologically. She had renal tuberculosis and a tuberculous fistula in ano. A search was made for Monilia, which was not seen at first but has since been observed in scrapings of the finger nails At times the eruption simulated psoriasis, and at other times avitaminosis was considered; in fact, the patient has had therapy for the latter condition. Originally Dr. Gross suggested the possibility that this patient had lichen scrofulosorum. I worked on that lead carefully and found that at that time she had lichen spinulosus. Several histologic sections showed this to be so. Apparently she was having a manifestation of lichen scrofulosorum of the so-called larval form. In other words, I have not been sure of the diagnosis, because of these evanescent lesions. Other physicians have said that lichen scrofulosorum shows these different manifestations: It will resemble psoriasis; it will have its papulonecrotic phases; it will follow other frank tuberculous manifestations. In fact, it may do any of the things which have occurred in this case. The lesion on the chin, which is only of four or five months' duration, has a definitely tuberculoid structure. Histologically, it was somewhat atypical for sarcoid. It has only been after many years of study of this woman that I have been able to make a definite diagnosis. In fact, a few weeks ago several lesions had many of the clinical characteristics of syphilis. I have instituted treatment to verify the diagnosis.

Sarcoid of Boeck (Generalized). Presented by DR. G. F. MACHACEK.

C. B. R., a Negress aged 29, is presented from the Vanderbilt Clinic, because of a generalized eruption of seven years' duration. She was born in New York city and at one time had treatment for "poor blood."

Examination shows nodules on the upper eyelids and dark pigmented nodules on the nose, which circumscribe the nostrils and ascend into the cutaneous cover of the septum. The lips are swollen, but no definite nodules are distinguished. Papules and comedos are scattered over the cheeks and the chin. Both hands show deep movable nodes on the dorsum near the wrist. All the fingers are swollen and spindled, and cutaneous nodular infiltrations are present. The finger nails are dystrophic and striated (of the right first, third and fourth and the left first, third, fourth and fifth fingers). There is a crusted area over the right elbow. There are atresia of the nasopharynx and hoarseness, and endoscopy shows the

epiglottis to be destroyed but healed. Ulcers of the mouth are noted. The liver is palpable and appears to be somewhat enlarged.

Roentgen examination disclosed cystic disease (sarcoid) of the bones of both hands and of the styloid processes of the ulnas. The bones of the feet showed decalcification. Roentgenograms of the lungs showed hilar shadows and exaggeration of the bronchovascular markings. Repeated examination of the sputum showed no acid-fast organisms. The blood count showed 4,000,000 red blood cells, 70 per cent hemoglobin and 4,500 white blood cells, with 60 per cent polymorphonuclear leukocytes. The Wassermann test with cholesterolized antigen gave a 2 plus reaction. Repeated examination of the urine showed albumin consistently; the specific gravity was low, averaging 1.013, and both hyaline and granular casts were present. The renal excretion was about 45 per cent according to the phenolsulfonphthalein test. Histologic examination of a cutaneous specimen excised from the nose showed sarcoid structure. A specimen removed from the buccal mucosa showed a chronic ulcer. The oral lesion showed Vincent's organisms in symbiosis.

There was no elevation of temperature. A salt-poor vitamin-rich diet was prescribed, vitamins being added in the form of cod liver oil. The nodules of the nose were electrodesiccated, and this resulted in some scarring.

DISCUSSION

DR. OSCAR L. LEVIN: This patient presented various lesions of tuberculosis and demonstrated the different reactions that may occur in the skin in association with such an infection. Among the lesions, some on the face, particularly on and about the nose, were fairly characteristic of lupus miliaris faciei, while others were fairly characteristic of tuberculosis papulonecrotica. Two lesions, one on the left cheek and one on the right lower eyelid, suggested sarcoid. Cystic lesions on the backs of the hands and the wrists and on the fingers were probably associated with tuberculosis of the small bones and characteristic of the lesions observed in Schaumann's disease. The roentgenogram of the lungs suggested sarcoidosis. It is advisable to recognize the fact that tuberculosis of the skin due to internal tuberculosis may manifest itself in multiform types of lesions on the skin in the same person. I do not know what the reaction to tuberculin in this case was, but the absence of a positive reaction would help to confirm the diagnosis of sarcoid. The pathologic picture of sarcoid is not the same in all cases and may vary from the classic picture of sarcoid to that of papulonecrotic tuberculid, that of erythema induratum and even that of a destructive form of lupus vulgaris.

DR. PAUL GROSS: It is a striking fact that in the majority of cases extensive sarcoid of the skin and the internal organs is seen in this country in Negroes. The peculiarity in the response of the Negro to tuberculosis has been expressed in recent literature by use of the title, "Tuberculosis of the Negro." His response to syphilis has also been referred to, particularly by Dr. Howard Fox. I can recall a case in which there was an eruption of the face resembling lupus miliaris and associated with hepatosplenomegaly and another in which lichen scrofulosorum was associated with extensive infiltration of the lungs. In both histologic examination of the cutaneous lesions showed typical sarcoid structure; the reaction to tuberculin with the lowest dilutions was negative. If the solution of the problem of sarcoid could be found, the biologic reasons for this unusual reaction of the Negro might be near.

DR. CHARLES WOLF: I agree entirely with Dr. Gross's conception of this condition as a particular type of tuberculosis which exists in the Negro. The race is not so important as the soil. In other words, if tuberculosis exists for a long time in a person, the reactions of immunity change; therefore, the types of tuberculosis vary and assume the various familiar forms. This concept has been demonstrated in white persons. Various manifestations of tuberculosis have developed in the same patient, tuberculous adenitis appearing in childhood, lupus erythematosus in adolescence and hilar and pulmonary tuberculosis later in life. Furthermore, lichen scrofulosorum appeared in some of these patients.

DR. G. F. MACHACEK: In a discussion of tuberculosis, for convenience and for certain prognostic advantages, the different forms must be classified. If precise classification is criticized on the one hand, I do not think, on the other hand, that proper names should be used. Dr. Wolf's statements are interesting. There is a changing immunity in cutaneous tuberculosis. Some patients with sarcoid-like tuberculosis and a negative reaction to tuberculin get along well and for one reason or another experience sudden improvement in their cutaneous lesions. Frank tuberculosis develops, however, and their general health deteriorates. The reaction to the tuberculin test at this time usually becomes positive. It must be considered that many of these patients have syphilis. Therapy for syphilis may in many ways influence the reactivity to tuberculin. Then, there's the pathetic economic status of many of these persons, particularly when they are sick and cannot work. As they frequently render personal services, no one will employ them when they are disfigured.

Unusual Eruption Suggestive of Vitamin B_2 Deficiency, Cured by Injections of Liver Extract. Presented by DR. PAUL GROSS.

E. T., a woman aged 29, is presented from the Vanderbilt Clinic. The patient was admitted on July 19, 1937, to the Presbyterian Hospital, on account of a generalized symmetric eruption. For four months before admission she had been working in a laundry and had felt overtired. She has headaches, nausea and dizziness and has been suffering for several years from constipation. Her diet consists largely of bread, macaroni and spaghetti, milk or cheese rarely, meat twice a week, a few green vegetables and no fruit.

At the time of admission her skin showed marked seborrhea of the scalp and a diffuse erythematous yellowish red scaly eruption on both ears and the eyebrows and in the nasolabial regions. The sides of the neck and the upper part of the back showed patches of small follicular papules. In the axillary folds were diffuse brownish red patches studded with small follicular papules with exfoliative centers. Both elbows, the waistline, the groin, the perianal region, the thighs and the knees showed large erythematous patches covered with silvery exfoliative scales, which remained within the borders of the lesions. The palms showed a diffuse keratotic thickening on an erythematous base, giving a yellowish waxy appearance. On the lateral surface and the dorsa of all the fingers were patches covered with scales resembling psoriasis. The eruption resembled in its different aspects pityriasis rubra pilaris, pellagra, seborrheic eczema and psoriasis, but none of these diagnoses was made; the condition was considered as an eruption sui generis, and a vitamin deficiency was suspected.

Examination of the blood showed 76 per cent hemoglobin, 4,040,000 red blood cells and 7,360 white blood cells. The Wassermann reaction was negative. Gastric analysis showed, during fasting, no free hydrochloric acid and total acid of 1.5; twenty minutes after administration of histamine, free hydrochloric acid of 28 and total acid of 34, and forty minutes after administration of histamine, no free hydrochloric acid and total acid of 1. Examination of the eyes by Dr. P. A. Carroll showed no abnormality except a high degree of myopia. Examination of the stools for Monilia gave negative results. Histologic examination of a specimen of tissue removed from the abdomen showed low grade dermatitis.

The patient received intramuscular injections of liver extract, and her condition showed marked improvement within two weeks. She was discharged from the hospital on August 6. Treatment has been discontinued since October 15, and she has returned to her regular occupation. A recent examination showed slight scaling over the elbows but no recurrence of the eruption.

DISCUSSION

DR. J. GARDNER HOPKINS: Dr. Gross has shown me several instances of this condition, which neither he nor I knows how to classify. It bears some resemblance to pellagra and some to seborrheic eczema, and sometimes there is this striking

response to liver therapy. I think the condition is important and ought to be more widely recognized.

DR. PAUL GROSS: The eruption in another of my patients resembled in every detail the condition described here tonight. After the patient had received a few injections of liver extract, this therapy was discontinued, and when I saw him a few weeks ago, he still showed marked hyperkeratosis of the palms and the soles and an erythematous scaly eruption on the body. He is now receiving an aqueous liver extract by mouth and has shown some improvement.

DR. HERMAN GOODMAN: The literature on dermatologic symptoms of avitaminosis is recent. I have recently reviewed all articles available and am convinced that it is impossible to distinguish clinical dermatologic entities as due to deficiency of any one individual vitamin. In the ordinary mode of living, no person is deprived of one vitamin. A woman on a reducing diet or a young girl with acne who has been ordered to abstain from certain foods cuts down on all the vitamins. The manifestations of vitamin deficiency on the skin become those of lack of several vitamins. A. Pasini (*Verhandl. d. internat. Kong. Dermat.* **2**:166, 1937) proposed the name dysvitaminoses cutanées, an excellent one for the use of clinicians. The patient presented by Dr. Gross showed evidence of lack of vitamins A and B_1, for example. Has she deprived herself of butter?

DR. G. F. MACHACEK: Avitaminosis can be secondary to an initial eruption. I have observed cases of established avitaminosis in hypersensitive persons, who first showed improvement only after injections of liver. It is plausible to consider the skin a storehouse and a site for the formation of vitamins. Hence, inflammation, oozing and desquamation may cause a secondary avitaminosis. The therapy may perhaps break this vicious cycle.

DR. PAUL GROSS: The patient received halibut liver oil, but only after she had shown definite improvement from liver therapy.

DR. GEORGE C. ANDREWS: I should like to mention 2 patients who were cured with liver extract. One was a shoe salesman who had been out of work for three years because his palms were so thickly hyperkeratotic that he could not move his hands enough to pick up bundles. He had keratotic lesions on the trunk, on the elbows and on the backs of the hands. There were keratotic papules on the knuckles, and the soles were thick. The condition resembled pityriasis rubra pilaris but was not typical of that disease. His mother had psoriasis. He had been on a diet of only potatoes, tea and bread for six months and before that on restricted diets. For years he had not eaten much meat or vegetables and was much underweight. I took him to the Rockefeller Institute, where he was studied and put on a liberal diet high in vitamins and given injections of liver. Inside six months he was back at work and remained well, gaining a great deal of weight. The other patient was a woman who had what is usually called neurodermatitis of the back of the neck and kraurosis vulvae. Because of the kraurosis vulvae, I thought of a vitamin deficiency. She had digestive trouble and vomited every day, so that what food she did eat she usually vomited. She was undernourished and underweight, with secondary anemia. The condition cleared during liver therapy and local treatment with weak tar ointments. I have heard since that she does not itch any more and is well.

Prurigo Nodularis. Presented by DR. ISADORE ROSEN.

T. K., a woman aged 52, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. An eruption of six years' duration is located chiefly on the lower extremities. It consists of elevated, bluish papules and nodules varying in size from that of a pea to that of a small coin; some of them are scaly. There are a few verrucous lesions on the palms. On the trunk there are scratched papular lesions.

On Dec. 11, 1937, the blood count was normal and urinalysis showed no abnormality. The congo red injection test on the left leg gave negative results.

There were 1,640 mg. of total lipids per hundred cubic centimeters, and partition showed 250 mg. of total cholesterol, 195 mg. of cholesterol esters and 55 mg. of free cholesterol, esters composing 78 per cent and free cholesterol 22 per cent of the total cholesterol; 10.7 mg. of lipid phosphorus, and 267 mg. of lecithin. The albumin-globulin ratio was 4.3:2.34. The histologic examination showed typical prurigo nodularis.

DISCUSSION

DR. R. H. RULISON: I think this case is a fine example of the disease. As Dr. Rosen pointed out, prurigo nodularis is seen infrequently, at least so far as my own experience is concerned.

DR. OSCAR L. LEVIN: I agree with the diagnosis. Examination of the blood showed a high cholesterol and a high fat content. It may be worth while in the future to study the blood of patients with prurigo nodularis, to see if there is a relation between the fat metabolism and the eruption.

Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi. Presented by DR. GEORGE C. ANDREWS.

M. E., a Jew aged 50, is presented from the Vanderbilt Clinic. Seven years ago a red to purple plaque developed on the medial side of his left ankle. During three years purple plaques and nodules varying in size from that of a dime to that of a dollar developed on each leg. The right ankle became involved with similar indurated plaques. The toes assumed a "frostbitten" appearance, which has persisted to the present itme. After three years irregularly outlined red to purple indurated plaques varying in size from that of a pea to that of a dollar developed on the thighs. During the past two or three years the trunk has become involved, and in the past year, the upper extremities and the face. The general health has always been good.

The toes vary from red to blue and are edematous. The ankles present marginated indurated purple plaques. Scattered over the legs and the thighs are irregularly outlined indurated plaques and nodules which vary in color from red to purple and in size from that of a pea to that of a dollar. Similar lesions are present on the wall of the chest, the hands and the forearms. The lobes of the ears are red and infiltrated. The eyelids are slightly pigmented. On the left side of the chin is a pea-sized red macule. The legs have been edematous in recent months, but are less so since frequent elevation has been practiced.

Histologic examination showed multiple idiopathic hemorrhagic sarcoma of Kaposi.

All the involved areas were treated with roentgen radiation (150 r), filtered through 3 mm. of aluminum, during the week of Dec. 20, 1937. Some improvement has been noted.

DISCUSSION

DR. DAVID BLOOM: I wish to call attention to the verrucous eruption on the dorsa of the toes, which may appear before any typical lesions of Kaposi's sarcoma.

A Case for Diagnosis (Scrofuloderma?): Secondary Radiodermatitis. Presented by DR. FRANK VERO.

P. H., a man aged 37, is presented from the Vanderbilt Clinic. About fifteen years ago he noticed a lump the size of half a dollar above the sternum; this opened spontaneously, discharging pus. The condition has been treated by various local measures and roentgen therapy in different hospitals and institutions throughout the country. It has never healed completely.

In the region of the sternum is a palm-sized area showing pseudoscleroderma-tous changes. The skin is hard, adherent to the underlying tissues, depigmented in the center and hyperpigmented at the periphery, with a few telangiectases and nodules throughout. Along the clavicle are numerous fistulas which discharge a yellowish thin seropurulent secretion. The areas surrounding the fistulas are

reddened, moist, eroded and crusted. The clavicular bones seem to be thickened. Above the clavicles there are two deeply retracted walnut-sized scars, appearing like hollow spaces.

The patient entered the clinic because of a generalized dermatitis, which soon disappeared.

The Wassermann reaction was negative. Microscopic examination and cultures showed no fungi. Inoculations of animals gave negative results. Roentgenograms of the sternum showed various-sized irregular areas of diminished density in the manubrium. There was one area of destruction along the upper anterior aspect of the sternal segment. Syphilitic gumma or one of the chronic granulomas, such as actinomycosis or blastomycosis, might produce this picture, and a chronic infectious osteomyelitic process is to be considered, although the osseous reaction usually seen in association with such a condition is not present. This picture has never been seen as a result of roentgen therapy. Tuberculosis should be considered and investigations made to rule it out.

Histologic examination showed dermatitis. Slight parakeratosis and hyperkeratosis were noted, with marked edema and moderate leukocytic infiltration of the epidermis. There was moderate acanthosis. The corium was extremely edematous and showed a profound pleomorphic infiltration of leukocytes, with large numbers of polymorphonuclears and plasma cells. No more definite diagnosis than that of cutaneous inflammation could be made.

DISCUSSION

DR. OSCAR L. LEVIN: The patient presents diffuse chronic radiodermatitis on the chest. It is impossible to say what was the original cutaneous disease from which the patient suffered. No evidences of tuberculosis are now present. The small nodules within the scar may be the beginning of cancer.

DR. G. F. MACHACEK: The histologic examination did not show anything typical except a marked chronic inflammatory reaction which was granulomatous, with some of the features of radiodermatitis. I do not know exactly what the underlying lesion might have been, but there are deep scars in the supraclavicular region and, I believe, in the suprasternal region.

Chancroid (Chancre?). Presented by DR. FELIX PHILIP LOWENFISH.

J. M., a man aged 34, is presented from the Vanderbilt Clinic because of a lesion on the penis of three months' duration.

Examination shows an elevated ulcerated oval thumb nail-sized lesion on the under surface of the penis, about 1 inch (2.5 cm.) behind the glans. The lesion is larger now than it was at the time of admission, Dec. 1, 1937. The floor of the ulcer is yellowish red, and the edges are rolled. Palpation indicates cartilaginous induration. There is no inguinal adenopathy. The patient previously received one injection of neoarsphenamine from a private physician.

Repeated dark field examinations and Wassermann tests have given negative results. Smears showed no Ducrey bacilli or Donovan bodies. Two Frei tests gave negative results and the Ito test a positive result. Histologic examination of two biopsy specimens showed (1) granulation tissue and (2) chronic ulcer. Treatment has consisted of application of wet dressings.

DISCUSSION

DR. DAVID BLOOM: I think the autoinoculation test may be of value.

DR. LOUIS TULIPAN: In spite of the fact that no Donovan bodies were observed, I suggest the diagnosis of granuloma inguinale. I think a single granulomatous lesion of the type present, with a smooth surface and a border which resembles epithelioma, is fairly typical and is seen especially in white patients. In the Negroes the lesion is more distinctive. I should suggest that the lesion be removed and many sections made from the base of the biopsy specimen. Donovan bodies then could probably be demonstrated.

DR. HOWARD FOX: It is probably too late to obtain successful autoinoculation in this case, as the lesion has been present for three months. It has been my experience at the Bellevue Hospital that after six weeks it is usually difficult or impossible to produce inoculation. The duration of three months does not exclude chancroid, as I have observed cases in which the disease was of long duration and in which the diagnosis was confirmed by the Ito test and by autoinoculation. I think this lesion is chancroid.

DR. G. F. MACHACEK: My impression from reviewing the histologic report is that the lesion is probably chancroid. Another possibility is granuloma inguinale. No Donovan bodies were observed, but, as Dr. Fox said, that is in no way final proof. Banal pyogenic infection must be considered.

DR. LOUIS CHARGIN: I suggest the use of sulfanilamide in this case. I have treated chancroid in a series of cases at the Department of Health Clinic, and in all cases the lesion cleared rapidly durnig its use. No local treatment except the preservation of cleanliness was employed. The procedure is well worth a trial.

DR. MARION B. SULZBERGER: "Dmelcos" is really a patent name for the vaccine which was discovered by Ito while he was working under C. Bruck in J. Jadassohn's clinic. I think the test should be called the Ito rather than the Dmelcos test. It is a specific test and if it really gave positive results in this case—and I presume it did from the presenter's statements—it makes necessary the assumption that this man either has had chancroid at some previous time or that the present lesion is chancroid. Moreover, I see no clinical feature which is incompatible with the diagnosis of elevated ulcus molle.

DR. G. F. MACHACEK: I was glad to hear Dr. Sulzberger's comments. Last year I posed the question of what the Dmelcos test was. It is the injection of a suspension of the killed Ducrey organisms and the correct full name is Ito-Reenstierna test.

DR. PAUL GROSS: If a mixed infection with syphilis can be absolutely ruled out, I prefer the diagnosis of ulcus molle elevatum to that of granuloma inguinale.

DR. SAMUEL M. PECK: My clinical conception of granuloma inguinale is that the base should be much more granulomatous and not so smooth as this is. Furthermore, Dr. Jerome Kingsbury and I (*J. A. M. A.* **87**:1900 [Dec. 4] 1926) reported a series of cases, including some of chancroid, in which there was a favorable response to medication with antimony and potassium tartrate, so that response cannot be used as a point of differential diagnosis.

DR. HOWARD FOX: Copper sulfate has been considered specific in the treatment of chancroid. When numerous agents are recommended for the treatment of a certain disease, no one as a rule is specific. My experience with copper sulfate has borne out this statement.

DR. G. F. MACHACEK: Several diagnoses must be considered. I remember 1 case of granuloma inguinale in which the lesion was an open ulcer. The patient had syphilis and a Ducrey infection, and finally smears showed Donovan bodies. It is not uncommon for a patient to have several venereal diseases at one time. Another patient had not only gonorrhea, a Ducrey infection and Vincent's infection but syphilis, all at the same location and at the same time.

DR. WILLIAM BAYARD LONG: How much sulfanilamide does Dr. Chargin use?

DR. LOUIS CHARGIN: The usual dose is 80 grains (5.17 Gm.) in divided doses for two days and 40 grains (2.59 Gm.) for from five to seven days thereafter.

Moniliasis. Presented by DR. FELIX PHILIP LOWENFISH.

J. H., a man aged 33, is presented from the Vanderbilt Clinic because of an eruption involving the external genitalia and the groin, of four months' duration.

Examination shows superficial erythematous vesicular scaly lesions, which began in the groin and then spread to the scrotum and the base of the penis.

Monilia albicans was obtained on direct smear and on culture. Urinalysis showed no abnormality.

DISCUSSION

DR. R. H. RULISON: What treatment is being used?

DR. FELIX PHILIP LOWENFISH: I first applied 2 per cent methylrosaniline in 50 per cent alcohol. That seemed to be irritating, so I changed to boric acid ointment. The latter medicament seems to be doing more good.

DR. MARION B. SULZBERGER: In reference to the treatment with boric acid, boric acid and sodium borate are nearly specific for infections with Monilia. A. Dósa (*Arch. f. Dermat. u. Syph.* **176**:261 [Dec.] 1937) described in vitro experiments confirming that well known clinical fact and showing the strong actions of boric acid and sodium borate on fungi. I have often used sodium borate in the treatment of moniliasis.

DR. G. F. MACHACEK: Perborate paste is used in monilial infections of the nails.

Syringocystoma. Presented by DR. LOUIS CHARGIN.

V. L., a Negress aged 26, states that an eruption appeared as small nodules on her chest about ten years ago. The lesions have increased in number and size, spreading to the back, the axillary regions, the lower part of the neck, the arms and the legs. They vary in size from that of a millet to that of a bean and are globular. The skin over them appeared normal. When palpated most of the lesions are firm, but some are cystic. The larger ones are freely movable, while the smaller ones are firmly attached to the skin. There have been no subjective symptoms. The patient suffers from asymptomatic syphilis, and the Wassermann reaction is positive.

Histologic examination showed a large cystic and empty cavity extending from the middle part of the cutis to the bottom of the section. The wall consisted of two layers of cuboidal cells and was surrounded by a sheath of connective tissue. The microscopic diagnosis was syringocystoma.

Angiokeratoma. Presented by DR. LESLIE PAXTON BARKER.

D. G., a man aged 43, was first seen in the dermatologic department of the Vanderbilt Clinic on Sept. 15, 1937, at which time he complained of severe scrotal pruritus of six months' duration. He had not noticed any lesions in this area. He had been under treatment in the neurologic department because of a parkinsonian syndrome of undetermined source.

Examination shows over the scrotum many pinhead-sized bluish red angioma-like lesions, some of which have a fine scale over the surface. The lesions are firm to the touch.

The histologic diagnosis was angiokeratoma with thrombosis.

Leukoderma Centrifugum Acquisitum of Sutton. Presented by DR. RICHARD JAMES KELLY.

R. L., a girl aged 6 years, is presented from the Vanderbilt Clinic. One and a half years ago the patient first noticed a white spot surrounding a brownish black mole under her chin. Later, another white spot about 3 or 4 mm. in diameter and with brownish pigment at its center appeared lateral to this. At about the same time a larger, whitish area appeared over each parietal region, and the hair became completely depigmented. About six months ago, other depigmented macules appeared in the left axilla and the left popliteal region, and a linear area of depigmentation about 4 inches (10 cm.) long appeared on the right arm. Pigmented lesions have been present on the right hip since birth. The general medical history was essentially irrelevant, and physical examination showed no abnormality.

Rosacea-like Tuberculid of Lewandowsky (Following Sunburn); Xanthelasma. Presented by DR. G. F. MACHACEK.

H. K., a woman aged 51, is presented from the Vanderbilt Clinic, because of an eruption on the cheeks and the chin, of six months' duration. This eruption

appeared after a severe sunburn. Tiny nodules are scattered throughout a flushed area involving the cheeks and the chin. Diascopic examination shows brownish spots.

Intradermal injection of 0.1 cc. of old tuberculin with a dilution of 1 : 1,000,000 and of 1 : 100,000 produced no reaction; with a dilution of 1 : 10,000 there was a 2 cm. reaction after forty-eight hours. Histologic examination showed a tuberculoid granuloma in the corium, which suggested a nodule of lupus.

After the injection of old tuberculin, the eruption began to improve, although no improvement was noted during roentgen therapy. Treatment was continued, with intradermal injections of 0.1 cc. each of 1 : 80,000 and 1 : 40,000 dilutions of old tuberculin and thereafter of 1 : 40,000 dilution at weekly intervals of six weeks. The eruption has continued to improve.

DISCUSSION

DR. MARION B. SULZBERGER: The presentation of this case brings to light the possible usefulness of the immune-biologic therapeutic effect of tuberculin. However, the diagnosis is not absolutely certain from the present appearance of the patient; moreover, sometimes spontaneous cure takes place in rosacea-like tuberculids. Nevertheless, in the series of cases reported by Dr. G. M. MacKee and me (ARCH. DERMAT. & SYPH. **31**:159 [Feb.] 1935) repeated injection of tuberculin proved in some instances to be an efficacious method of therapy. I have been able to substantiate this observation in additional cases. Therefore, I think that in rosacea-like and other types of tuberculid injections of a gold preparation and of tuberculin are worth trying. I have followed some of these cases for as long as three years and have seen recurrences in some of them after a year or two. If one administers the therapeutic injections of tuberculin intracutaneously, one can follow the course of the cutaneous sensitivity. In some cases one can change the level of that sensitivity, producing a definite increase or decrease. Often, but by no means always, clearing of the cutaneous lesions is concomitant with the reduction of sensitivity to tuberculin. Another remarkable thing is that often, when a patient is retested with tuberculin after an interval—and sometimes coincidental with a recurrence of the tuberculid—one finds that the sensitivity to tuberculin has returned to its original level. I think that such unequivocal proof of successful specific hyposensitization of the skin to tuberculin is an extremely important addition to the knowledge not only of tuberculosis but of immune-biologic mechanisms in general.

DR. G. F. MACHACEK: If anything, the patient's sensitivity has increased. She is now reacting to 0.1 cc. of tuberculin with a dilution of 1 : 40,000, and previously she reacted only to 0.1 cc. of tuberculin with a dilution of 1 : 10,000. Although the case was presented as one of rosacea-like tuberculid of Lewandowsky, I was not certain that lupus miliaris disseminatus faciei should not be considered as a diagnosis. It is my understanding that in that condition the patient is even less sensitive to tuberculin than in Lewandowsky's rosacea-like tuberculid.

Lichen Planus Hypertrophicus. Presented by DR. S. M. KAUFMAN.

Dermatitis Herpetiformis. Presented by DR. BEATRICE M. KESTEN.

Rosacea-like Tuberculid of Lewandowsky (Following Sunburn). Presented by DR. G. F. MACHACEK.

Scleroderma. Presented by DR. FRANK VERO.

Morphea. Presented by DR. FRANK VERO.

A Case of Diagnosis (Nevus? Rhinophyma?). Presented by DR. LESLIE PAXTON BARKER.

Papulonecrotic Tuberculid. Presented by DR. G. F. MACHACEK.

Recklinghausen's Disease. Presented by DR. LEWIS B. ROBINSON.

LOUIS CHARGIN, M.D., *Chairman*

Feb. 1, 1938

HARRY C. SAUNDERS, M.D., *Secretary*

Sarcoidosis (Besnier-Boeck-Schaumann Syndrome) Involving the Skin, the Lymph Nodes, the Bones and the Tendon Sheaths. Presented by DR. WILLIAM LEIFER.

R. H., a Negress aged 25, married and childless, is presented from the Mount Sinai Hospital. She was first studied in April 1936, at which time there were lesions on the face similar to but smaller than those now present and lesions on the extensor aspects of the extremities. A clinical diagnosis of lupus miliaris disseminatus faciei and papulonecrotic tuberculid in a patient with late asymptomatic syphilis was made. The histologic studies confirmed the diagnosis of papulonecrotic tuberculid, but the tissue from the face revealed a picture "more suggestive of sarcoid." Intradermally injection of tuberculin with dilutions of 1 : 1,000,000 and 1 : 100,000 gave no reaction. The blood count was normal, and the Wassermann reaction was positive. Roentgenograms of the hands and wrists showed no changes in the bones. A roentgenogram of the chest showed "infiltration at the root of the right lung and enlargement of the right paratracheal glands. The picture suggested Hodgkin's disease."

The patient was given some organic and inorganic arsenic, but she soon disappeared from observation. She now states that all the cutaneous lesions disappeared without further therapy but have been returning gradually in the past four months.

Examination shows lesions distributed generally on the auricles, the face, the lips, the trunk, the buttocks, the extremities and the fingers. They are roughly of two types, the more numerous being papules and plaquelike lesions varying in size from that of a pinhead to larger than a silver dollar. These raised lesions are rounded or flat, firm and the color of skin or darker; some show yellowish flecks. On the face several are depressed and hyperpigmented centrally. The second type, on the outer aspects of the arms and on the buttocks, are firm nodules in the skin and attached to it. None of them are ulcerated. In addition, there are generalized adenopathy, with a rather disproportionate enlargement of the epitrochlear glands, and soft painless swellings about the dorsal tendons of both wrists.

An intradermal tuberculin test with a dilution of 1 : 1,000 and a patch test with tuberculin gave negative results. Blood count and urinalysis showed no abnormality. The Wassermann reaction was positive. A roentgenogram of the chest showed "distinct diminution in size of the paratracheal glands since the last examination (April 1936). The right hilar glands were still moderately enlarged, but less so than before." A roentgenogram of the bones showed a cystlike area in the distal shaft of the proximal phalanx of the right middle finger. Similar changes were seen in the proximal ends of the middle phalanx of the right index finger and of the terminal phalanges of the three middle digits of the left hand. There was a similar change in the lower end of the left ulna.

Histologically, a plaque on the right arm showed changes in the epidermis which were unimportant. The greater portion of the cutis was occupied by sharply circumscribed accumulations of epithelioid cells. In the edge of one of these lobules there were a number of Langhans giant cells. A lesion on the face showed practically the same picture, except that there were more giant cells. The histologic diagnosis was sarcoid of Boeck.

DISCUSSION

DR. MARION B. SULZBERGER: I think the eruption is fairly characteristic of Boeck's sarcoid and that the findings in the internal organs, the bones and so forth, are consistent with the diagnosis of generalized sarcoidosis or whatever

name the members agree to use. I think it is necessary to call the attention—certainly not of this particular audience, but of the medical profession in general—to the fact that patients with sarcoid often have lesions in the internal organs as well as in the skin. This is by no means a new observation. The generalized nature of sarcoidosis has long been known to dermatologists. Prof. J. Jadassohn told me many years ago that he believed involvement of the spleen was the most common internal manifestation of sarcoid and that involvement of the lungs or of the bones was not as common. He taught that one must always look for an enlargement of the spleen in cases of sarcoid, as well as study the roentgenograms of the bones, the lungs, etc. The thesis that sarcoid is a reaction of the tissue of a certain immunologic type is today well founded, and it is well established that sarcoid forms occur in leprosy, syphilis and other infections. Moreover, in a representative number of cases the cause of sarcoid is as yet unknown. In spite of this, it is apparent that in another large group the disease is related to tuberculosis. This is proved by many experimental and clinical observations, among which I shall mention only the clinical combinations with, and the transitions to, forms of classic cutaneous and internal tuberculosis. For example, papulonecrotic tuberculid in association with sarcoid is rare but still frequent enough to make one feel that the two conditions may be manifestations of different immunologic reactions of the tissue to one and the same etiologic factor. Moreover, true tuberculosis of he skin, such as lupus vulgaris, may be found in association with sarcoid, and one even sees transition, often with corresponding changes in sensitivity to tuberculin from the anergic sarcoid reaction to the hyperergic lupus reaction and vice versa. It is my experience that systemic sarcoidosis is in most cases tuberculous, and I believe the sarcoid reaction of the tissue may be found in cases of internal tuberculosis even in the absence of cutaneous sarcoid; when this reaction appears in the lungs, examination of the sputum and bacteriologic tests usually give negative results, and the course is relatively benign.

In this case sufficient testing has not yet been done to justify speaking with certainty of a real anergy to tuberculin. I should like to ask investigators studying cases of sarcoid in which there is a negative reaction to Koch's old tuberculin with a dilution of 1:1,000 to proceed with higher concentrations. One should be able to demonstrate a negative reaction with a 1:100 and even a 1:10 dilution of old tuberculin before one speaks of anergy. Too many normal persons fail to react to old tuberculin with a dilution of 1:1,000 to justify considering such failure a proof of specific anergy.

DR. OSCAR L. LEVIN: This case is another instance of a disease to which I called attention at the last meeting (ARCH. DERMAT. & SYPH., this issue, p. 449). I tried to emphasize the fact that in tuberculosis the eruption is polymorphous. Schaumann described a syndrome of which the essentials were the presence of sarcoid of Boeck in the skin, involvement of the lymph nodes and of the tonsil, the presence of osteitis tuberculosa multiplex cystoides and a negative reaction to tuberculin. The spleen and the liver may be involved, and the lungs may show a peculiar marbling on roentgen examination. In all cases of tuberculosis of the skin one must bear in mind that the cutaneous lesions may be of different types, depending on the reaction of the tissues to the tubercle bacillus.

DR. ISADORE ROSEN: I should like to hear from some of the members whether they have followed any case of this type long enough to know what the outcome is.

DR. DAVID BLOOM: The clinical picture presented by this patient is characteristic of tuberculosis of the skin in the Negro. I have never seen and have rarely read of an eruption like this in a white patient. I have often seen eruptions of this type in Negroes at the meetings of societies and have read of them. This fact is probably due to a special immunity in the Negro. The picture is characteristic. There are tiny nodules on the eyelids, at the alae nasi and on and near the lips and larger nodules or plaques, sometimes resembling lupus erythematosus, on the rest of the skin. Frequently keloid-like lesions are seen, as in this case, the picture on the neck and the antecubital regions. The lungs are more

or less involved, sometimes suggesting advanced pulmonary tuberculosis. Frequently the lymph glands are enlarged. In spite of extensive dissemination of the disease, strangely, the patients seem to be in fairly good general condition and may live for a long time. The lesions may persist or undergo involution, leaving scars. However, in some cases this quiescent infection may flare and appear as active pulmonary tuberculosis, as in the case reported by J. V. Klauder and F. D. Weidman (*Dermat. Wchnschr.* **99**:1665, 1934), in which the autopsy showed tuberculosis of the lungs with caseation and intestinal tuberculosis. The reaction to the tuberculin test, which may be negative for a long time, may change to positive. I assume that the general treatment for tuberculosis will go a long way to prevent an acute flaring up and breaking down of the immunity.

DR. G. F. MACHACEK: I brought out a few points at the last two meetings about sarcoid. I mentioned the fact that physicians consider this a new disease, and I brought out the point about generalization. It appears that immunity and hypersensitiveness do not go hand in hand. As far as the outcome of this disease is concerned, of several cases which I had an opportunity to observe and which were presented here, other tuberculous manifestations developed in 2. In 1 there was tuberculous osteitis. The patient became sensitive to tuberculin, and her sarcoids disappeared. In other words, her cutaneous disease improved but her general condition became worse. In the other case pleurisy with effusion developed. At that time the sarcoids disappeared. A physician extracted part of the pleural fluid and reinjected it, after which the patient felt better; her pleurisy with effusion disappeared, but the sarcoids came back. In that case tuberculosis was not definitely proved, bacteriologically, but in the first case it was.

DR. OSCAR L. LEVIN: In regard to the question asked by Dr. Rosen, as to the prognosis of this disease, I may say that the patient progresses surprisingly well when placed in the proper environment, with good food, good housing and plenty of sunshine and fresh air. It is worth while noting that tuberculosis of the skin responds well to ultraviolet radiation, and in my experience at the Sea View Hospital, Staten Island, N. Y., in over five years, I found that most tuberculous conditions of the skin tend to disappear when exposed to ultraviolet radiation, with doses beginning at only two or three minutes and gradually increasing until the patient is able to stand a dose of two or three hours twice a week. Not only does the skin improve, but so does the general condition.

DR. MARION B. SULZBERGER: In regard to Dr. Rosen's question, I should like to express agreement with Dr. Levin's prognosis. I have, in general, found the outlook good when sarcoidosis is treated as tuberculous. However, the prognosis is not good in all cases, and sarcoid not infrequently mutates to progressive and open tuberculosis, if the patient is not treated and if he follows his ordinary daily pursuits. My experience shows that some patients with general sarcoidosis get well; in some the condition remains stationary, even for decades, and in some progressive tuberculosis of the internal organs develops. This is true in cases of sarcoidosis of the lungs and other internal organs, even when not associated with cutaneous lesions.

DR. LOUIS CHARGIN: It is important to note that not infrequently when the eruption disappears some form of active tuberculosis is developing and that when the active tuberculosis disappears the sarcoid eruption frequently recurs. Another important point is that if the reaction to the tuberculin test of patients suffering from sarcoid becomes strongly positive, active tuberculosis is most likely developing. With respect to the remarks of Dr. Bloom, while sarcoid seems to be common in Negroes, it is certainly observed in white persons.

DR. WILLIAM LEIFER: I should like to call attention to the fact that in the article by W. T. Longcope and J. W. Pierson (*Bull. Johns Hopkins Hosp.* **60**: 223, 1937) all the 8 patients reported on were Negroes. In fact, most of the cases in the American literature have occurred in Negroes. I think that this is interesting, in view of the fact that the cases originally studied and reported in the Scandinavian literature were in white patients exclusively. There must be

some similar alteration of cellular reaction in these two distinct racial groups which produces this typical clinical syndrome.

Progressive Cutaneous Vascular Disease, with Hemorrhage by Diapedesis. Presented by DR. SAMUEL M. PECK.

B. S., a woman aged 29, born in Russia, is presented from the Mount Sinai Hospital. The changes in the skin began about nine years ago as black and blue discolorations on the legs. Three years ago they began to appear on the arms. The skin generally has a cyanotic appearance, with many cutaneous vessels plainly visible on stasis, giving the impression of an exaggerated picture of cutis marmorata on the body and acrocyanosis on the extremities. Especially on the arms and the legs the dilated vessels are definitely visible, and the lower portions of the legs almost show varicose dilatation. In addition, on the limbs are scattered areas of ecchymosis, some fresh and some old. On the right leg is an old scar about 5 cm. in diameter, which is the result of trauma. No atrophy is seen accompanying the dilatation.

The Wassermann reaction was negative. Chemical examination of the blood showed 275 mg. of cholesterol, 6.8 mg. of total protein and 5.2 mg. of albumin. The tourniquet test and the venom test gave negative results. A blood count showed 108 per cent hemoglobin, 5,100,000 red blood cells, 8,000 white blood cells and 200,000 platelets.

Histologic examination showed the epidermis to be somewhat atrophic. Throughout the cutis, especially in the upper portion, were many dilated small vessels (practically telangiectatic) and a great deal of fresh and old hemorrhage. The endothelial cells themselves were flattened, showing no necrotic changes, but the spaces between the endothelial cells were markedly widened. In places hemorrhage by diapedesis was evident. This was not due to a vitamin C deficiency, in spite of the histologic resemblance of the mechanism of hemorrhage to that condition. The ingestion of vitamin C is apparently of normal amount. No determination of the excretion of vitamin C was made.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: The patient's eruption began after her last pregnancy. Since then her menstrual periods have been irregular, and obesity has developed. The polycythemia is significant, and she has headaches. This suggests the syndrome described by Harvey Cushing (*Bull. Johns Hopkins Hosp.* **50**:137, 1932; J. A. M. A. **99**:281 [July 23] 1932) in basophilic adenoma of the anterior lobe of the pituitary body.

DR. OSCAR L. LEVIN: The patient is apparently suffering from an endocrine disorder. Some of the cutaneous lesions resemble those described by Cushing in basophilic adenoma of the pituitary gland. In fact, 1 patient in the group described by him, whom I also saw, had cutaneous changes resembling some of those in the patient presented this evening. A complete examination of the patient's skin could not be made this evening, and a search for more of the signs of Cushing's disease was not possible. I believe a more careful and thorough examination may disclose that the patient is suffering from a disease of the glands of internal secretion. The color of the skin is a peculiar dusky red and resembles that observed at times in acrodermatitis chronica atrophicans as well as in Cushing's disease.

DR. ISADORE ROSEN: I was much interested in this case because of the close resemblance of the condition, at a glance, to acrodermatitis chronica atrophicans. However, after careful examination one can readily rule out that condition. There is a strong resemblance in this case to one shown at a meeting of this society some time ago by the late Dr. Goldenberg. That patient was suffering from polycythaemia vera and had a generalized vascular disturbance. She had a strongly positive Wassermann reaction and was treated for syphilis. After treatment for a long time the vascular condition improved.

DR. SAMUEL M. PECK: I should like first to apologize for the name under which this case was presented. I thought it was a mechanistic description of

what was happening. When first examined, the patient appears to have acrodermatitis chronica atrophicans, but she does not. The color is partly due to the patient's tendency to polycythemia. The hemoglobin content is 108 per cent. The patient has edema of the legs and no real clinical atrophy. The most interesting part of the histologic picture is that it resembles scurvy (there is hemorrhage due to diapedesis). There is no inflammatory reaction. There is secondary degeneration of elastic tissue such as would be seen in any case of long-standing hemorrhgae. There is no capillary fragility in the true sense, in which there is weakness of the endothelial cells. I do not know what the condition is. Perhaps it is due to an endocrine disturbance.

A Case for Diagnosis (Leprosy?). Presented by DR. PAUL GROSS, for DR. LUDWIG SCHWARZSCHILD.

D. L., a woman aged 44, is presented from the Hospital for Joint Diseases, where she was first seen on Jan. 26, 1938. She has an eruption, which began one and one-half years ago on the legs and became generalized during the past four or five months. She complains of itching. She was born in the republic of Colombia and has lived in the United States since 1922, with the exception of half a year in Panama and two years in Puerto Rico. In 1926 she was given two courses of arsphenamine and a bismuth preparation at the Lenox Hill Hospital, because of a positive Wassermann reaction. She was married in 1922 and has had no pregnancies. She has been suffering from disease of the gallbladder since 1935.

The eruption consists of bluish red nodules of firm consistency varying in size from that of a pea to that of a dime. Many of these are elevated, with a round top and often a shiny surface. Others form flat cutaneous nodes, and some are sharply circumscribed subcutaneous infiltrated lesions. Over the lower part of the right shin is a grayish yellow hypertrophic lesion of somewhat sclerodermatous consistency. Scattered on the arms and the legs are reddish nodules, firmer than the others and resembling keloids. The chin shows slight diffuse infiltration, with several papular lesions. The lymph glands are not enlarged. The ulnar nerves are of normal thickness.

Urinalysis showed a specific gravity of 1.033, with an acid reaction, a faint trace of albumin and no sugar. Examination of the blood showed 14.2 Gm. of hemoglobin, 4,160,000 red blood cells and 10,800 white blood cells, with a differential count of 82 per cent neutrophils, 1 per cent eosinophils, 15 per cent lymphocytes and 2 per cent monocytes. The Wassermann reaction has not been reported yet. A nasal smear did not reveal any Hansen's bacilli. Histologic examination showed changes suggestive of leprosy (nodular type).

DISCUSSION

DR. HOWARD FOX: I think this case is unquestionably one of leprosy. A probable diagnosis could be made from the appearance of the hands, which show pigmentation and wrinkling of the skin of the dorsal surface and swelling of the fingers. The yellowish red nodules of various sizes on the extensor surfaces of the upper extremities are characteristic. The histologic report of xanthoma makes me think that the changes were confused with those of leprosy.

DR. E. WILLIAM ABRAMOWITZ: I agree with the diagnosis of leprosy.

DR. A. W. GRACE: A good test as to whether tissue contains the acid-fast bacilli of leprosy is to make a smear from a biopsy specimen before it is placed in the fixative and stain the smear with the Ziehl-Neelsen stain. The acid-fast bacilli can be observed in such a smear.

DR. PAUL GROSS: I agree with Dr. Grace that a direct smear from the lesions should have been made, and the omission was due to technical difficulties. I had the impression that I was dealing with a sarcoid type rather than the pure nodular type of leprosy.

NOTE.—Staining of the histologic section and of the direct smear from the lesion showed numerous Hansen bacilli.

Dermatitis Medicamentosa (Due to Injections of Liver?). Presented by Dr. Samuel M. Peck.

R. K., a woman aged 60, presented from the Mount Sinai Hospital, has been under observation since 1934 because of nontropical sprue; she has been receiving liver therapy by intramuscular injection in doses of 2 cc. for the past three years. Her hands have been dry since 1934, when she was seen by me for this condition. About three weeks ago an acute papulovesicular eruption suddenly developed on the arms, the face and the neck. One of the last injections of liver was reported to have caused a great deal of pain. It was given rather superficially.

When the acute eruption developed, a patch test was applied to the "v" area of the chest, where she was free of lesions. A week later an acute vesicular eruption developed on the area where the patch test had been applied. This is still present. A patch test on the thigh four days ago gave a negative result.

The Wassermann reaction was negative. The icterus index was 10. The Rehfuss test meal showed 22 degrees of free acid in the stomach. Because of the hyperchromatic condition of the blood and the presence of free acid in the stomach, it was felt that the patient had nontropical sprue rather than pernicious anemia.

The problem at present is as to continuance of the liver therapy. It is important to decide whether the injections of liver had anything to do with the development of this eruption, because the blood picture of nontropical sprue will again develop if liver therapy is withheld for any length of time. The patient is presented for an opinion as to whether one can rule out the diagnosis of dermatitis medicamentosa due to liver therapy and continue the injections of liver. I do not know just what preservative was used by the manufacturer in the preparation of the liver extract.

DISCUSSION

Dr. E. William Abramowitz: In some cases infantile eczema has been attributed to cod liver oil. As far as I know, there are no reports of such an extensive dermatitis following the intramuscular injection of a liver preparation. Local induration, urticaria and at times general symptoms of shock, attributed to the histamine content of the earlier products, have been reported occasionally. In this particular case some other contaminant may be responsible for the dermatitis.

Dr. Paul Gross: I am always skeptical when one considers eczematoid dermatitis a drug eruption. The only exceptions are arsphenamine dermatitis, eruptions due to other heavy metals and eruptions in which sensitization from without has taken place before the drug was given internally (quinine dermatitis). The eruption in this patient strongly suggests contact dermatitis. I have never observed any eruption after injections of liver.

Dr. Henry D. Niles: If one saw this patient without knowing the history, one would make a diagnosis of contact dermatitis. There are scaling, erythema and edema, and the eruption is limited to the exposed areas of the arms, the neck and the face. It is hard, as Dr. Gross has said, to conceive of the eruption's being due to an intravenous injection, particularly since it is so limited. There is no eruption on the covered areas of the body. I questioned the patient carefully about external irritants but could not get a history of any. The eruption did not appear on all these areas at the same time. The patient told me it appeared on the left arm first, later on the right arm and still later on the face. I should like to have a more careful study of the case for the possibility of external irritants.

Dr. Marion B. Sulzberger: From the appearance and the localization of the dermatitis, I should first consider a dress dye as a possible factor. Dr. Joseph Goodman and I have recently published an article on this subject (*J. Allergy* **9**:136, 1938). As for liver's causing an eczematous eruption, in the last analysis liver is one of the foods as well as a medicament. In many years of patch testing with foods I have yet to see a positive reaction to a patch test with a food—that is, when the "protein" ordinary excitant fraction is used as material for the patch test. One often gets a positive reaction to a patch test with rind of orange

or with a vegetable with which the patient comes in contact, but in these instances not the protein but some other fraction produces the eczematous eruption. I have even obtained fat-solvent extracts, thinking that perhaps some eczematous eruptions were due to the fat-solvent–soluble fractions of foods, but even with these I have not obtained any conclusive positive reactions to patch tests. Therefore, I may be permitted the important conclusion that there is no evidence that an eczematous eruption of true contact type can be produced by the ingestion of food. If such eruptions occur, they must be exceedingly rare and therefore of little clinical importance. However, I recall 1 case of pernicious anemia in which an eczematous eruption developed on the dorsa of both hands after injections of liver. An exacerbation followed each injection, and improvement ensued when the injections were omitted. The patch tests with liver extract gave negative results in my case, and I had no opportunity to find the responsible ingredient (preservative, etc.).

Dr. G. F. Machacek: I observed a case of contact urticaria from eggs. I cannot remember, however, which part of the egg caused the reaction, the lipoid part of the yolk or the white. The patient was an egg candler, and the case involved compensation. The patient reacted to the albumin.

Dr. Eugene F. Traub: My conception of this case is similar to that of the previous speakers. I doubt whether there is any direct connection between the injections of liver and the eruption, but it is possible that the fixative or preservative used in the preparation of the liver extract was responsible. This point may be of importance if the liver injections are to be continued. It might be possible by simply changing the brand of the preparation used to get away from the offending agent. The possibility that the patient may actually be sensitive to the liver extract should not be entirely ruled out, however, as such sensitivity has been reported.

Dr. Samuel M. Peck: I admit that this eruption has by no means been proved to be due to liver extract. Since the patient really needs the liver therapy, I am glad to know that most of the members present think it has no connection with the eruption. Therefore, I shall continue the injections. I shall continue to use the same brand of extract and see if the eruption gets worse. I do not believe that Dr. Sulzberger meant that foods cannot cause an eczematous eruption. Eczema in children has been proved many times, I think, to be due to foods. I have obtained positive reactions to patch tests with wheat in eczema in children.

Dr. Marion B. Sulzberger: In reply to Dr. Peck: I believe—and I am sure it is the consensus today—that infantile eczema is not considered the equivalent of contact dermatitis. When I spoke of "eczema" in relation to foods, I referred only to contact dermatitis and not to infantile eczema, to neurodermatitis, to atopic dermatitis or to other forms. I think it is important for all the members to agree that the ingestion of foods has so far never been proved to be of etiologic significance in the production of contact dermatitis in adults.

Purpuric Leukemid in a Case of Chronic Myelogenous Leukemia. Presented by Dr. Samuel M. Peck.

A. F., a woman aged 50, presented from the Mount Sinai Hospital, has been complaining for the last eight years of weakness, shortness of breath and generalized itching. For about the same period she has had a peculiar pigmentation, which began around the legs and has since been progressively ascending toward the pelvis. On both legs are numerous brownish red macules of various sizes and ages, which do not disappear under pressure and which are evidently purpuric spots. The eruption is limited to the legs. On the arms and the abdomen are a number of scratch marks. The complexion is sallow. The only other eruption noted is a pinguecula of the right inner canthus.

Physical examination showed the blood pressure to be 212 systolic and 100 diastolic. The heart is enlarged and shows a systolic murmur. The spleen and

the liver are markedly enlarged. Lymph nodes are not palpable. Ophthalmoscopic examination showed sclerotic vessels and a small hemorrhage on the left macula lutea.

The Wassermann reaction was negative. The pinch and the tourniquet test gave positive results. Chemical analysis of the blood showed 4.9 mg. of albumin and 2.8 mg. of globulin, making the total protein content 7.7 mg., per hundred cubic centimeters. A blood count showed 2,150,000 red blood cells, 47 per cent hemoglobin and 6,700 white blood cells, with a differential count of 54 per cent segmented forms, 2 per cent lymphocytes, 5 per cent monocytes, 38 per cent myelocytes and 1 per cent myeloblasts. The platelet count showed 120,000. Sternal puncture yielded fluid containing a total of 45,000 white blood cells, and a slightly increased number of erythroid elements. A test of hepatic function with sodium benzoate showed 0.185 Gm. of benzoic acid in four hours.

The case is presented as one of leukemid because, although there has not been a histologic examination, the condition does not look like leukaemia cutis and cannot be classified as the purpura which often complicates leukemia when the bone marrow is involved.

DISCUSSION

DR. MARION B. SULZBERGER: Would Dr. Peck classify this condition as leukemid if the histologic examination showed no leukemic infiltration? My conception is that the name "leukemid" should be applied, if at all, only to a leukemic picture in the skin which is secondary or hematogenous; and that primary leukemia of the skin is that in which leukemic changes are found in the skin before they are found in the blood or elsewhere. Primary cutaneous leukemia is rare, and the disseminated lesions one usually finds are apparently due to hematogenous distribution and could perhaps be called "leukemid," although the term is at best apt to be misleading.

DR. CHARLES WOLF: The concept of leukemid was first brought forward by C. Audry (*Ann. de dermat. et syph.* **3**:310, 1902). He differentiated between leukemia of the skin and leukemid. Leukemid is a manifestation in the skin with a histologic picture of nonleukemic infiltration and an inflammatory reaction in the cutis, whereas in leukemia of the skin there is an infiltration of the type of cells characteristic of the type of leukemia from which the patient is suffering, either myelocytes or lymphocytes. Therefore, the term "leukemid" should be retained for eruptions produced by a toxic reaction. In other words, leukemids and leukemic infiltrations will occur during treatment with roentgen rays and independently of treatment, and the two types of manifestation may occur at the same time.

DR. PAUL GROSS: To make the discussion complete, one has to mention the exanthematous type of reaction in leukemia, described by L. Arzt (*Arch. f. Dermat. u. Syph.* **160**:84, 1930). I believe that is what Dr. Sulzberger had in mind.

DR. MAX SCHEER: To emphasize what has been said before, I think Dr. Wolf's conception is the correct one. In leukemia cutis there is leukemic infiltration in the skin, which is demonstrable histologically. Leukemid is a nonspecific eruption which takes various clinical forms, such as papules, wheals, etc., and is histologically nonspecific; it may be found in cases of leukemia. It is to these nonspecific eruptions that the term leukemid has been applied, I believe, by Audry and others.

DR. HOWARD FOX: I agree entirely with what Dr. Wolf has said. The term leukemid is unfortunate. It should be analogous to the terms syphilid and leprid, which denote lesions caused by Spirochaeta pallida and the leprosy bacillus, respectively. The term leukemid should be applied to the true leukemic infiltration and not, as is the custom, to the nonspecific toxic eruption.

DR. SAMUEL M. PECK: Drs. Fox, Wolf and Scheer are right, according to the accepted practice in naming these manifestations. The fact that a general term such as leukemid designates the nonspecific eruption in Hodgkins' disease, leukemia and other blood dyscrasies speaks for itself on the specificity. Histo-

logically, sharply circumscribed lymphocytic accumulations are most often seen around blood vessels. I think that the eruption which this patient presents can be called a real leukemid because it is purpuric, toxic and nonspecific.

Epidermolysis Bullosa. Presented by DR. WILLIAM LEIFER.

C. S., a school girl aged 17, born in the United States, is presented from the Mount Sinai Hospital. She states that "blisters" were noted for the first time when she was 15 days old and have been present intermittently since then, particularly at such sites of pressure as the palms and the fingers after she uses a broom, the feet, the lower part of the thigh when she has worn a tight circular garter and the area around the waist when she has worn tight clothing. Large bullous lesions in those areas have been observed during her attendance at the clinic.

Examination shows large clear bullae springing from a noninflammatory base and healing without scarring but leaving hyperpigmentation. There are no epidermal cysts and no evidence of dystrophic changes.

The patient's parents are not consanguineous, and no other member of the family has a similar condition.

A blood count showed 91 per cent hemoglobin, 9,950 white blood cells and a differential count of 67 per cent neutrophils, 25 per cent lymphocytes, 6 per cent monocytes, 1 per cent basophils and 1 per cent eosinophils. The Wassermann reaction was negative. Urinalysis showed no abnormality. Histologic examination of skin from the abdomen (stained with hematoxylin and eosin) showed an increase of pigment in the basal cells, some dilatation of the vessels and slight perivascular infiltration in the upper part of the cutis. Elastic tissue fibers were absent in the papillary layer.

DISCUSSION

DR. PAUL GROSS: It is significant that this patient states that she has more blisters on the feet during the summer. This is frequently true in cases of nondystrophic epidermolysis bullosa and apparently has something to do with the perspiration.

DR. LOUIS CHARGIN: In some cases of this disease hematoporphyrin has been found in the urine, and I suggest that it be looked for in this case. Cases have been reported in which bullous lesions of epidermolysis followed mild sunburn. Perhaps there is some relation between this sensitivity to light and the presence of hematoporphyrin in the urine.

DR. LOUIS TULIPAN: It is interesting to note that simple epidermolysis bullosa usually clears up by the time the patient has reached this girl's age. It is unusual for lesions to continue developing in a patient of her age.

Mycosis Fungoides. Presented by DR. EUGENE F. TRAUB.

B. G., a woman aged 39, has been under treatment at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for the past ten years. The original eruption consisted of peculiar reddish brown plaques involving the face and the upper part of the trunk. There was no itchy prodromal eruption, and there never has been an eczematoid or psoriasiform eruption. The process began as an infiltrated plaque but tumors tended to form rapidly. The eruption has been kept under control with roentgen therapy, but whether this treatment prevented the formation of tumors is not known. Despite the fact that the patient has received more or less constant roentgen therapy for eleven years, no signs of roentgen dermatitis have so far developed.

The case is presented for therapeutic suggestions, especially as to the advisability of further roentgen treatment.

DISCUSSION

DR. CHARLES WOLF: Dr. Traub asked whether further treatment with roentgen rays should be administered in this case. Not knowing the exact dose

she has received, I might say that so far the roentgen rays have done no visible damage to the skin. In further roentgen therapy, I should administer massive doses. I think these lesions could be easily cleared up by doses of 500 r with a 3 mm. aluminum filter at one sitting. I should like to suggest to Dr. Traub that he try this treatment on one patch. Radiodermatitis will not develop.

DR. LOUIS CHARGIN: What is the effect of such a large dose on the bone marrow?

DR. CHARLES WOLF: First of all, these particular patches are not in the locations of the long bones. They are in the axilla, along the ribs. After one large dose there might be a temporary leukopenia, but after a little rest the leukocyte count would come right back to normal.

DR. E. WILLIAM ABRAMOWITZ: A patient originally seen by Dr. George H. Fox some forty years ago went to many dermatologists and finally came into my hands. He was still in the second stage of mycosis fungoides. Most of the dermatologists had followed the roentgen technic advised by G. M. MacKee. The eruption always responded to 75 roentgens. I think this indicates that it is not a rational procedure to use a large dose of roentgen rays when a small dose is sufficient.

Mucous Cysts of the Mucous Membrane of the Hard Palate. Presented by DR. CHARLES WOLF.

P. F., a man aged 54, is presented from the Mount Sinai Hospital. On the anterior third of the mucous membrane of the hard palate are several raised lesions, shiny and yellowish red. They are arranged in the shape of a garland. On the left side there is a split pea-sized lesion which is slightly ulcerated. On the right side of the median line some of the lesions appear cystic, and pressure produces a sense of fluctuation. Puncture elicits a gelatin-like material. There is no pain. The patient wore a denture for six years but has not used it for the past eight months. The lesions first appeared four months ago and have showed no change.

The Wassermann reaction was negative. Histologic examination showed a chronic inflammation, with epithelial hyperplasia.

DISCUSSION

DR. GEORGE M. LEWIS: A somewhat similar condition of the hard palate was described by H. Orr (*Brit. J. Dermat.* **42**:436 [Oct.] 1930). In 2 instances the disease disappeared when the patient quit smoking.

DR. CHARLES WOLF: When I first saw these lesions, there was a circinate arrangement, and they strongly suggested the possibility of syphilis. However, the Wassermann reaction was negative. Further observation showed discrete cysts, and puncture produced a gelatinous fluid. Microscopic examination revealed nothing unusual, except an inflammatory process with hyperplasia. The diagnosis at the present time is mucous cysts. The condition has improved somewhat during local treatment by washing the mouth with sodium perborate.

Pityriasis Rosea with Vesicles, Including the Face. Presented by DR. NATHAN SOBEL.

K. K., a boy aged 12 years, is presented from the Mount Sinai Hospital because of an eruption of twelve days' duration. The lesions are generalized and consist of pea-sized and larger erythematous pink macules, some showing vesicles and some, typical scaling. On the face the lesions are the size of a pinhead and larger. The case is presented because of the vesicular character of the eruption and the extensive involvement of the face.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I made a diagnosis of pityriasis lichenoides before I learned the history. However, after further examination I admit the possibility of pityriasis rosea.

DR. OSCAR L. LEVIN: The lesions suggest pityriasis rosea, and I believe the patient is suffering from this condition. However, it is possible that pityriasis lichenoides of Juliusberg may develop. This eruption has been present for only twelve days, too short a time to allow for a definite conclusion as to the ultimate picture.

DR. ISADORE ROSEN: The case is presented because the condition is atypical. I have seen pityriasis rosea on the face and on the scalp. In one instance I saw lesions on the tongue, the palms and the soles, which cleared up with the regression of the cutaneous eruption.

DR. NATHAN SOBEL: When I first saw this boy, four days ago, there were more vesicular lesions than there are tonight. Some of the lesions on the face have cleared in the interim.

Macular Atrophy (Schwenninger-Buzzi Type). Presented by DR. SAMUEL FELDMAN.

A. M., a Negress aged 21, was presented before the Bronx Dermatological Society on Jan. 27, 1938 (ARCH. DERMAT. & SYPH. **38**:117 [July] 1938).

DISCUSSION

DR. SAMUEL FELDMAN: The case is interesting because of the presence of early lesions. On the back are a few lesions no larger than a pinhead. These are somewhat raised and firm. The lesion next in size is flat and not so firm. The lesions tend to follow the lines of cleavage. There has been no syphilis, tuberculosis or other disease in either the patient or her family. There was no cutaneous disease or inflammation preceding this eruption, and the condition has never been accompanied with any symptoms. Under the microscope, no change appeared in the epithelium, aside from slight thinning and flattening. The cutis was edematous, particularly in the upper layers. The elastic tissue was almost completely missing. The entire picture was typical of the Schwenninger-Buzzi type of macular atrophy.

A Case for Diagnosis (Macular Atrophy Secondary to Syphilis?). Presented by DR. LOUIS CHARGIN.

L. P., a Negress aged 31, married, is presented from the Central Social Hygiene Clinic, because of an eruption on the abdomen and the back, which, according to the patient's statement, has been present for ten years. She has asymptomatic syphilis. It is impossible to ascertain the age of the syphilitic infection and, therefore, to trace its relation to the macular atrophic areas. The lesions are mainly on the abdomen and the back. They vary from the size of a pea to that of a dime and are isolated and confluent. The lesions exhibit the usual characteristics, some being somewhat solid but many showing herniation. They are skin colored. There are no subjective symptoms.

In view of the facts that the lesions are typical of macular atrophy and that the patient has syphilis, it is assumed that the eruption is a secondary type of macular atrophy following a former syphilitic eruption.

DISCUSSION

DR. SAMUEL FELDMAN: There is a difference in the clinical appearance of the lesions in the case presented by Dr. Chargin and the case I presented. In Dr. Chargin's case the lesions are soft but stippled and resemble pock marks, while in my case the surface of the lesions is wrinkled.

Fixed Eruption Due to Acetarsone. Presented by DR. LOUIS CHARGIN.

F. C., a man aged 45, is presented from the Central Social Hygiene Clinic. He has suffered from syphilis since 1933. The fixed eruption first appeared

one and one-half years ago, after the twenty-fourth injection of arsphenamine. Since then he has been found to be sensitive to silver arsphenamine, sulfarsphenamine, neoarsphenamine, acetarsone, alvarsone (Dermatological Research Laboratories) and mapharsen. He has given a negative reaction to tryparsamide, phenolphthalein and antipyrine. The eruption is scattered over the body and is of the fixed type especially seen after administration of preparations of the arsphenamine-phenolphthalein-phenobarbital group. Of further interest is the fact that little pigmentation is associated with the eruption.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: The patient presents a typical fixed or focal eruption. It is no longer believed that phenolphthalein is the only drug which produces this type of lesion. Dr. M. H. Noun and I (ARCH. DERMAT. & SYPH. **35**:874 [May] 1937) have indicated that about fifteeen different drugs can produce similar manifestations, which makes it impossible to determine by simply looking at the eruption which of the various drugs is responsible.

DR. MARION B. SULZBERER: Was the acetarsone given by mouth?

DR. LOUIS CHARGIN: The acetarsone was given by mouth. On a former occasion the patient was given nine tablets of 0.25 grains (0.016 Gm.) each, and he responded with a flare-up. The second six tablets were taken at the rate of three a day. After the second dose the eruption began to flare up.

DR. MARION B. SULZBERGER: In the first place, I think the specificity or lack of specificity of the eruption is interesting. I believe in many cases arsphenamine dermatitis and arsphenamine hypersensitivity of various types are not produced by arsenic but by certain characteristic chemical groupings to which the arsenic is attached. It is thus incorrect to speak of "arsenical" dermatitis in such cases. The patient is not sensitive to arsenic in the same way that patients are sensitive to mercury in the mercurial eruptions or to bismuth in bismuth dermatitis. Furthermore, I think it is interesting that here one has proof, if one still needs it, that some active portion of the acetarsone is absorbed from the gastrointestinal tract, and one need not be astonished by its effect therapeutically when given by mouth. I should like to ask the presenter to continue his investigations with tests with certain other inorganic arsenical preparations, such as sodium arsenate and potassium arsenite.

DR. LOUIS CHARGIN: I have tested a number of patients who were sensitive to the arsphenamine group of arsenical preparations with the inorganic arsenical compounds. In no case was any lighting up of the eruption produced by the inorganic arsenical compounds.

Xanthomatosis (Generalized); Hepatomegaly Associated with Jaundice; Tertiary Syphilis. Presented by DR. E. WILLIAM ABRAMOWITZ, for DR. JACOB SKEER, Brooklyn.

L. C., a Negress aged 39, came to the clinic of the Jewish Hospital in Brooklyn on March 22, 1937, because of jaundice and an eruption. In 1935 the patient was told that her eyes were turning yellow, and she went to the clinic of a hospital in Savannah, Ga., where she was told she had a large liver and a 4 plus Wassermann reaction. She received six intravenous injections, one each week, and then, because of increased icterus, medication was discontinued. At about this time she noticed the appearance of a generalized eruption accompanied with itching. In March 1937 the Wassermann reaction was positive. She has lost 22 pounds (10 Kg.) in the past year.

Examination on March 22, 1937, showed yellowish firm velvety tumefactions on the upper and lower eyelids, extending onto the cheeks, the ears and the chin. The neck and all the flexor surfaces (the axillas, the cubital spaces, the groin and the popliteal spaces) had large plaques made up of nodules varying in size from that of a pinhead to that of a pea. There were linear streaks on the palms and

small nodules on the areolas of the breasts. The conjunctivas were jaundiced. The liver was enlarged 2 fingerbreadths below the umbilicus and was hard and smooth. There were discrete papules with excoriated tops, the result of scratching due to jaundice. She was admitted to the hospital on March 29, 1937.

A roentgenogram of the chest showed a suggestion of thickening of the pleura at the base of the left lung. The cardiac shadow was apparently within normal limits. The aortic arch was slightly dilated. Roentgenograms of the gastrointestinal tract showed evidence of incompetency of the ileocecal valve. A roentgenogram of the tibia showed a definite ripple of the cortex of the lower portion of the right fibula, suggesting the presence of productive periostitis. An electrocardiogram showed deviation of the axis to the left with a regular sinal rhythm and a rate of 100. Examination of the spinal fluid showed no abnormality. The reaction to the Kline test was 2 plus on March 31 and on April 6. The Wassermann reaction was negative. Tyrosine was found in the bile. Examination of the feces for blood gave a 4 plus result on April 3 but subsequently gave negative results. Urinalysis showed no albumin, sugar or arsenic; urobilinogen (in a 1:20 dilution of urine), 3 plus to 2 plus; bile, 3 plus to trace. A blood count on March 30, 1937, showed 4,180,000 red blood cells with 70 per cent hemoglobin and 9,400 white blood cells, with 78 per cent polymorphonuclear leukocytes, 20 per cent lymphocytes and 2 per cent monocytes; there was a decrease in the number of platelets. On April 2 a blood count showed a normal number of platelets and a differential count of 62 per cent polymorphonuclear leukocytes, 31 per cent lymphocytes, 1 per cent eosinophils and 5 per cent monocytes.

Chemical studies of the blood showed an icterus index of 33.4 and 23.6, by direct and by indirect tests, respectively. Bromsulphalein and galactose tolerance tests gave positive results. The values for sugar in the dextrose tolerance test were: at 8:10 a. m., blood, 103 mg. per hundred cubic centimeters, and urine, none; at 8:55 a. m., blood, 215 mg., and urine, none; at 9:55 a. m., blood 270 mg., and urine, 0.46 per cent and at 10:55 a. m., blood, 248 mg., and urine, 0.28 per cent. The total protein content of the blood on one occasion was 7.69 mg. per hundred cubic centimeters (1.97 mg. of albumin and 5.72 mg. of globulin for an albumin-globulin ratio of 0.34) and on another occasion 7.95 mg. (2.29 mg. of albumin and 5.68 mg. of globulin, for an albumin-globulin ratio of 0.40). The total cholesterol of the blood amounted to 736 and later 615 mg. per hundred cubic centimeters; the free cholesterol, 337, and the phosphatase, to 25 and 30 units.

Histologic examination showed groups of large cells with vesicular nuclei and foamy granular cytoplasm in the corium. The histologic diagnosis was xanthoma.

At present the lesions have subsided to a marked degree. Jaundice and hepatomegaly still persist.

Fox-Fordyce Disease. Presented by DR. NATHAN SOBEL.

C. C., a woman aged 26, is presented from the Mount Sinai Hospital because of an eruption involving the axillas, the breasts, the umbilicus and the groins, of two years' duration. The eruption consists of extremely pruritic pigmented pinhead-sized flat papules, some of which are follicular. The histologic diagnosis was Fox-Fordyce disease. In the spring of 1936 the patient received four weekly roentgen treatments, each consisting of 140 r filtered through 3 mm. of aluminum. There was no improvement.

Generalized Lichen Planus with Involvement of the Nails and Ulcerations of the Buccal Mucous Membrane. Presented by DR. CHARLES WOLF.

Lymphogranuloma Venereum. Presented by DR. LOUIS CHARGIN, for DR. B. A. KORNBLITH.

Syphilitic Glossitis (Showing Malignant Changes?). Presented by Dr. Louis Chargin.

Multiple Superficial Basal Cell Epithelioma; Radiodermatitis. Presented by Dr. Lewis A. Goldberger.

Psoriasis Resembling Lichen Planus. Presented by Dr. Nathan Sobel.

Secondary Syphilis (Resistant). Presented by Dr. Nathan Sobel.

Lupus Erythematosus and Chronic Radiodermatitis. Presented by Dr. Louis Chargin.

Naevus Papillomatosus. Presented by Dr. Henry D. Niles.

Louis Chargin, M.D., *Chairman*

March 1, 1938

Harry C. Saunders, M.D., *Secretary*

Lichen Planus; Secondary Syphilis. Presented by Dr. Leo Spiegel.

I. G., a fireman aged 33, married, states that during the early part of August 1937 he was treated for sore throat, cervical adenitis and pain and swelling of the ankles and wrists. A gland from the neck was removed; microscopic examination revealed inflammatory tissue only. A few weeks later he was admitted to the Lenox Hill Hospital because of severe pains in his joints, and he had a profuse papular syphiloderm. There was generalized adenopathy, most evident in the left cervical region. The Wassermann test with two antigens gave a 4 plus result. He received three intramuscular injections of a bismuth preparation and three intravenous injections of 0.2 Gm. of silver arsphenamine during his ten day stay in the hospital. After this therapy he was referred to the outpatient department for continued treatment.

Since coming under observation he has received twelve intravenous injections of silver arsphenamine, six intravenous injections of 0.3 Gm. of old arsphenamine and twenty-one intramuscular injections of cyclobis (bismuth camphenilamate). On Feb. 24, 1938, the Wassermann test with two antigens gave a negative result, as did the Kline precipitation test with both diagnostic and exclusion antigens. On January 17 he complained of itching and called attention to a rash which he stated had been present a few days. Examination showed an acute generalized erythematous eruption, which was diagnosed as pityriasis rosea. Numerous lesions were also present on the palms and the soles. These lesions varied in size from that of a pinhead to that of a pea and larger, forming circinate patches. Many of them were raised, hyperkeratotic and centrally depressed and suggested arsenical keratoses.

About two weeks later the entire eruption took on a different aspect, especially on the trunk and the extremities, many of the lesions, especially on the forearms, becoming circinate, shiny, umbilicated and in some areas scaly. Numerous lesions were now observed on the lips, the buccal mucous membranes and the penis.

In my opinion, this patient had uncured latent syphilis, and acute lichen planus, which originally looked like pityriasis rosea, developed.

Note.—A biopsy subsequently verified the diagnosis of lichen planus.

DISCUSSION

DR. OSCAR L. LEVIN: The patient has an eruption with the clinical characteristics of lichen planus. There are some lesions, for instance those on the front of the right shoulder and the upper part of the right side of the chest, which suggest pityriasis rosea, but when closely studied they prove to be lichen planus. The lesions on the palms are definitely lichen planus and are not due to arsenic. The rapid development of the negative Wassermann reaction may be due to the production of antibodies by the severe reaction in the skin (in a manner similar to that observed in esophylaxis).

DR. HERMAN GOODMAN: When one considers the multiplicity of lesions and the possibilities mentioned, of pityriasis rosea, lichen planus, syphiloderm and arsenical eruption, the only answer is parapsoriasis.

DR. OSCAR L. LEVIN: It is possible that the injection of a bismuth preparation may have caused the atypical appearance of this eruption.

DR. MARION B. SULZBERGER: In this case there are many characteristics of typical lichen planus, which can often start in atypical fashion. One sometimes finds great difficulty in differentiating between early lichen planus and dermatitis venenata, seborrheic eczema or pityriasis rosea. In other words, although lichen planus is supposed to consist essentially of the characteristic papule, the early or prodromal eruptions are often uncharacteristic, and one can make the diagnosis only after a period of observation. In regard to the atypical, erythematous, scaly and itchy eruptions which are occasionally seen before true lichen planus, I have often wondered whether some of these may not be dermatoses from other causes which then act as isomorphic effects of irritation (Koebner) in making quiescent lichen planus appear as a sequela. An interesting point in this case is the development of lichen planus during the administration of two drugs which are used for the treatment of the disease. One must seriously consider the possibility that these drugs produced the eruption, rather than that the eruption became atypical because of the use of these drugs. Lichen planus-like eruptions can be, and often are, produced by drugs, particularly by arsenical preparations.

DR. ADOLPH ROSTENBERG: I had a case in which the picture could not be differentiated from typical pityriasis rosea, and after a few weeks it looked like lichen planus. The strange thing is that after another few weeks it again looked like pityriasis rosea and it ended by looking like lichen planus. My theory is that these lesions are due to the administration of arsphenamine. Pityriasis rosea cannot be absolutely excluded in this case.

DR. E. WILLIAM ABRAMOWITZ: In view of the fact that this eruption at one time looked like pityriasis rosea and now resembles lichen planus, and as the patient had received two heavy metals that are known to produce both pityriasis rosea-like lesions and lichen planus (and they are not the only such preparations which can produce such lesions), I think it can be assumed logically that the patient had a pityriasis rosea-like eruption, which has been described frequently after the administration of arsphenamine and bismuth, that evolved into a lichen planus-like eruption, which is also known to occur after the use of arsphenamine. The question is: was the condition typical pityriasis rosea? The pityriasis rosea-like eruptions after administration of heavy metals are not typical. The herald patch is missing. The duration of the eruption is much greater, and itching may be pronounced. The diagnosis of drug eruption would account for the various phases of the eruption observed in this case.

DR. LEO SPIEGEL: There was no evidence of a primary patch of pityriasis rosea. The eruption developed during antisyphilitic therapy. The patient states the rash has been getting better, especially during the past two weeks. He is receiving a bismuth preparation at weekly intervals.

Lichenoid Arsenical Dermatitis. Presented by DR. HARRY C. SAUNDERS.

L. S., a man aged 37, presented from the Bellevue Hospital, was previously shown at a meeting of the Manhattan Dermatologic Society on Feb. 8, 1938 (ARCH. DERMAT. & SYPH. **38**:114 [July] 1938).

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: In some ways this case can be compared to Dr. Spiegel's case. I believe there was probably a lichen planus-like eruption that left intense pigmentation. There is decided lichen spinulosus of the trunk, to which I should like to call attention. This is known sometimes to be a part of the clinical picture of lichen planus. Whether or not hairs will return in those patches on the scalp is questionable. If atrophy should develop, it would be interesting, because E. G. G. Little (*Brit. J. Dermat.* **27**:183, 1915) has called attention to lichen spinulosus of the body with atrophic areas of the scalp.

A Case for Diagnosis (Kaposi's Sarcoma?). Presented by DR. DAVID BLOOM.

J. H., a man aged 64, presented from the Bellevue Hospital, has been previously shown before the Manhattan Dermatologic Society, on Jan. 11, 1938 (ARCH. DERMAT. & SYPH. **37**:918 [May] 1938), the New York Dermatological Society, on Jan. 25, 1938, and the Bronx Dermatological Society, on Feb. 24, 1938 (ibid. **38**:124 [July] 1938).

Since the last presentation, violaceous, slightly infiltrated, irregularly shaped plaques varying in size from that of a dime to that of a half-dollar have appeared, disappeared and reappeared. They are nonpruritic.

After two weeks' medication with solution of potassium arsenite the tumors on the extremities have flattened considerably, and the lesions on the neck have shown considerable involution.

DISCUSSION

DR. PAUL E. BECHET: I am interested to learn that some of the sections strongly resemble Kaposi's sarcoma, because I suggested the possibility of that diagnosis when the patient was presented before the Manhattan Dermatologic Society. A large plaque on the heel was sharply defined and violaceous, with involvement of the blood vessels, and was typical of Kaposi's sarcoma. The nodules on the thighs were most atypical; in fact, their appearance did not in the least resemble idiopathic multiple hemorrhagic sarcoma. The short duration was also against the diagnosis.

DR. DAVID BLOOM: I believe that Kaposi's sarcoma is the most likely diagnosis clinically and pathologically. Particularly the appearance of the lesions on the lower extremities, the complete lack of subjective symptoms and the moderate eosinophilia would fit into this diagnosis. The fact that the lesions appeared first on the face and neck and later on the extremities and the nationality of the patient (a native American of Irish descent) do not speak against the diagnosis.

Epidermolysis Bullosa Hereditaria. Presented by DR. DAVID BLOOM.

W. D., a boy aged 15, presented from the Bellevue Hospital, was born in the United States of Czecho-Slovakian parents. Since early childhood he has complained of bullae following injury. On both elbows there are crusted lesions, the results of dried bullae. On the dorsa of the hands, the knees, the legs and the ankles are numerous atrophic scars resulting from previous bullous lesions. In many of the scars tiny epidermal cysts are seen. Some of the nails are deformed, shortened or absent. The patient states that the finger nails fall off from time to time. An older brother, aged 21, has similar dystrophic nails. Three other brothers and a sister are well. There is no history of consanguinity. The blood and the differential count were normal. The Wassermann reaction was negative.

DISCUSSION

DR. OSCAR L. LEVIN: The patient presents typical epidermolysis bullosa of the hereditary type. The family history indicates that a brother has a similar condition. Clinically, there are now present the characteristic lesions in the usual spots, old scars, areas of atrophy, epithelial cysts and denuded moist spots where bullae have been torn.

DR. CHARLES WOLF: It seems that the disease is at the stage of spontaneous involution. There are no active lesions at present. Epidermolysis bullosa hereditaria has a tendency after puberty to become arrested. At the present time this patient shows only the atrophic and milia-like lesions which are the end results of this disease. The probability is that active lesions will be more difficult to bring out on slight trauma than when he was younger.

DR. DAVID BLOOM: The patient presents active lesions, for the crusts on the elbows and the knees are the result of dried bullae. He has been under my observation for only a short time, but there is a history of gradual attenuation of the eruption since infancy.

Scleroderma and Hypertrichosis in a Child. Presentd by DR. DAVID BLOOM.

J. W., a girl aged 5 years, was previously presented before the New York Dermatological Society on Oct. 26, 1937 (ARCH. DERMAT. & SYPH. **37**:892 [May] 1938).

DISCUSSION

DR. MARION B. SULZBERGER: I agree with the diagnosis as far as the lesion on the side of the neck and the ear is concerned. This case is perhaps of the type in which one has the impression that therapy has helped, because this form of scleroderma tends to regress spontaneously, even sometimes to cure. However, I fail to see how in this particular case the ear can ever return to its normal size. I do not agree with the diagnosis of hypertrichosis and keratosis pilaris. One sees some hair on the child's back and arms and some keratosis pilaris, but I do not think it is of sufficient degree to justify calling the condition a cutaneous disease or, rather, two cutaneous diseases. In other words, I believe if one were to examine a series of normal children one would find a high percentage of children with as much hair as this child has and as much keratosis pilaris.

DR. E. WILLIAM ABRAMOWITZ: I am inclined to agree with Dr. Sulzberger that there is no connection between the scleroderma and the lesions on the body. I also agree that the amount of hairiness on the child's arms may be considered more or less normal. Female persons may have a slightly excessive amount ot hair on the body, especially lanugo, which is not considered an abnormality from the endocrine standpoint. If the condition were real hypertrichosis, it would be associated with some ovarian tumor. I do not believe the child shows any signs of such a condition. The interesting point, if the mother's statement can be believed, is that the child was born with a large amount of hair on the scalp and on the back, which disappeared when the child was a few months old. That manifestation has also been reported and has no great significance. I believe, therefore, that the condition here is probably scleroderma, and if there is any endocrine causation it probably is associated with the thyroid or the parathyroid gland.

DR. HERMAN GOODMAN: I think treatment of the parathyroid gland is indicated, because of the sclerodermatous condition of the ear. I agree with Drs. Sulzberger and Abramowitz that the amount of hair is not excessive. In most children who have an excessive amount of lanugo at the time of birth, the hair disappears before the child reaches adulthood.

DR. FRANK VERO: I have treated scleroderma in about 25 cases during the past few years, and reported the results in a discussion on Sellei's paper at the International Congress of Dermatology in Budapest, Hungary, in 1935.

In the treatment of circumscribed scleroderma I used mostly pancreatin. In some cases I used pepsin, hydrochloric acid and raw pancreas, which last substance many patients could not tolerate. In several cases I noticed a clearing up of the lesions; in some cases there was improvement, and in some instances new lesions appeared during the treatment. I have not seen any results from injections of Padutin alone in cases of circumscribed scleroderma. I could not hospitalize the patients and carry out all the treatment advised by Sellei. He modified his original method of treatment by administering desiccated hog's stomach, duodenin, preparations of liver, vitamins and heavy metallic preparations. His results with this treatment in the cases presented at the International Congress were astonishing.

In the treatment of diffuse scleroderma and sclerodactylia I have used injections of pancreatic extract in addition to pancreatin, raw pancreas, pepsin and hydrochloric acid. Some good results were obtained, although there were hardly any benefits when contractures of the fingers were present. In 2 cases ganglionectomy and sympathectomy had been done previously, but there was no improvement; in fact, in 1 case the condition progressed further.

It is difficult to follow cases of this disease for years, since the patient comes for treatment for a while and then discontinues treatment. Follow-up letters do not seem to be of any help.

DR. DAVID BLOOM: The congenital defect of the ear and the hypertrichosis, associated with circumscribed scleroderma, seem to me to be of significance. However, endocrine examination and roentgen study of the skull and the sella turcica did not show any abnormality. I have administered pancreatin to the child but did not see any effect from this treatment. I have observed several cases of morphea which has undergone involution without any treatment. If the disease improves after administration of pancreatin, I should hesitate to attribute the result to the drug.

Fixed Eruption in a Patient Sensitive to Arsphenamine and Phenolphthalein in Different Areas. Presented by DR. LOUIS CHARGIN.

C. M., a housewife aged 35, has had syphilis for about ten years. After the nineteenth injection of arsphenamine a fixed eruption developed. Subsequent testing showed her to be sensitive to neoarsphenamine and acetarsone but not to silver arsphenamine and sulfarsphenamine. Tests with other drugs which produce fixed eruptions showed sensitivity to phenolphthalein but in different areas from those affected by arsphenamine. The arsphenamine-sensitive areas are located chiefly on the left arm, while the phenolphthalein-sensitive areas are on the right side of the neck and the right arm. The patient is not sensitive to antipyrine.

At present the patient shows an activated fixed eruption on the right side of the neck and on the right arm which followed the ingestion of several tablets of ex-lax. The arsphenamine-pigmented areas on the left arm have remained unaffected.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I think this case is exceedingly interesting. The first report of fixed drug eruption was made by Ehrmann, who attributed the condition to menstruation. That was before antipyrine was introduced. When antipyrine and aminopyrine came into use, such lesions following the use of these drugs were reported by Brocq, who gave them the name "fixed eruption." After that Naegeli reported that arsphenamine produced the same type of eruption. Now reports indicate that besides the drugs mentioned previously, acetophenetidin, acriflavine hydrochloride, antimony and potassium tartrate, acetylarsan, mapharsen, tryparsamide, barbiturates, bismuth salts, cinchophen, iodides, ipecac, ipomea, isacen, mercury, phenolphthalein, quinine and acetylsalicylic acid have produced various types of fixed eruptions. The fact that mild mercurous chloride and bismuth have produced a fixed eruption raises a doubt as to the significance of the benzene ring in the composition of the other organic synthetic drugs. There

have been reports that psychic disturbances, foods, liquors and vaccines may sometimes cause these eruptions. They may occur spontaneously; that is, eruptions have been reported to appear after one or another of these various drugs and then to reappear apparently without the drug's being taken again. Now the chairman presents a patient in whom a fixed eruption developed in certain spots after the administration of arsphenamine and in other spots after administration of phenolphthalein. Only the arsphenamine-sensitive areas flared up after administration of arsphenamine, and only the phenolphthalein-sensitive areas flared up after administration of phenolphthalein. I think this is the first observation of its kind in the literature, and it is an important one. It may be of some help in tracking down the nature of this interesting type of cutaneous lesion.

DR. MARION B. SULZBERGER: I agree with everything that Dr. Abramowitz has said about this case. Other cases may exist, but it is difficult to find them, and I think that the presenter is to be complimented on the fact that he has proved that some of the lesions regularly flare up after the administration of one of the drugs and not after the other drug, while other lesions conduct themselves in a diametrically opposed manner. I should like to ask how often one sees a fixed drug eruption in which the same areas flare up with two different drugs? In a few cases I have seen a flare-up of phenolphthalein-sensitive sites after the taking of phenobarbital or a reaction successively to arsphenamine and to phenolphthalein in the same site. I think dermatologists have a great deal to learn about these fixed eruptions, and I do not think any one knows their exact mechanism or the precise site or seat of the effects. I should like to point out that, as both Dr. Abramowitz and the chairman have frequently told the members, these eruptions are often erratic—that is, the sites sometimes fail to flare up at all, even after administration of the actual causal drug. In other cases only a few sites and not all sites flare up. The sensitive areas seem to have a cyclic sensitivity to the drug, with variable periods of greatly increased and of greatly decreased local sensitivity. I think it is extremely important to keep this fact in mind, because it makes clear that one cannot say that a drug has not produced an eruption simply because one or more clinical trials of that drug fail to produce a flare-up of the lesions. These sites may be refractory for a long period, even to the drug which actually produced the original manifestations.

DR. HERMAN GOODMAN: I feel that this case is unique, and I am happy to have observed it. It seems to prove the specificity of the eruption to these two drugs. It adds to the hope that if study is continued others like it will be observed.

DR. E. WILLIAM ABRAMOWITZ: There have been a few reports of cases in which phenobarbital and drugs like eucalyptus have caused a fixed eruption. It is impossible to produce a fixed eruption in an animal. S. R. Rosenthal has been able to produce hypersensitivity to phenolphthalein in animals.

DR. LOUIS CHARGIN: This case is the only one of double sensitivity in different areas that I have ever observed, and by this time I have observed a considerable number of cases of sensitivity to arsphenamine, to phenolphthalein and to antipyrine, and I have seen an arsphenamine eruption activated by the intramuscular injection of bismuth subsalicylate. Dr. Sulzberger's observation that the fixed eruptions are erratic in their response to the drugs is accurate. Sometimes a large dose is required to activate the eruptions; at other times a small dose is adequate. Sometimes the response is to each treatment; at other times there are free intervals.

DR. CHARLES WOLF: May I make a suggestion, in view of the fact that the presenter has the opportunity of making these investigations? I feel there is some chemical relation between arsphenamine, phenolphthalein and antipyrine. They have a benzene ring. Patients whose lesions flare up during arsphenamine therapy give a history of having taken phenolphthalein at some time or other. I suggest that in a series of cases phenolphthalein be administered for a number of weeks at periodic intervals. And that arsphenamine be administered at the same time. I believe that fixed eruptions will be more frequent than they are ordinarily. I feel

that a fair percentage of patients in whom a fixed eruption develops after administration of arsphenamine have had a background of ingestion of phenolphthalein.

DR. LOUIS CHARGIN: In answer to Dr. Wolf, I should like to state that I have now a series of about 50 cases of fixed eruption due to arsphenamine. Every patient has been tested with antipyrine and with phenolphthalein, and the only case of double sensitivity in different areas is the one demonstrated this evening. In addition, 1 patient is sensitive to antipyrine and arsphenamine but apparently in the same areas—that is, antipyrine activates the arsphenamine-sensitive areas.

Chancroid, Cured with Sulfanilamide; Lymphogranuloma Venereum; Syphilis. Presented by DR. LOUIS CHARGIN.

S. E., a man aged 39, is presented for Dr. Borris A. Kornblith, from the Central Venereal Disease Clinic, Bureau of Social Hygiene. The patient had a pustule at the urethral meatus of which dark field examination on June 1, 1936, gave a negative result. The Wassermann reaction was 4 plus. The lesion ulcerated and involved the entire glans, with sloughing through the urethra in spite of antisyphilitic treatment until September 1937. Repeated smears for the Ducrey bacillus, the Ito-Reenstierna test and the Frei test gave positive results.

The patient has received antisyphilitic treatment since June 1936. The Wassermann reaction in January 1938 was 3 plus. He received Frei antigen intravenously on Oct. 10 and Nov. 5, 1936. He was given ten doses of 5 cc. of antimony and potassium tartrate (1 per cent), and cauterization with nitric acid, phenol and iodoform and ether was done. All the methods of treatment described were of no avail. From Sept. 18 to Oct. 2, 1937, a total of 760 grains (49.28 Gm.) of sulfanilamide was administered, and the lesion healed entirely in two weeks. There has been no recurrence.

DISCUSSION

DR. BORRIS A. KORNBLITH (by invitation): There have been 24 cases of proved chancroid in Dr. Chargin's clinic at the Department of Health. In 23 the lesions healed within two weeks after the treatment was begun. The total dose was 45 Gm. in two weeks. In other words, the dose was 80 grains (5.18 Gm.) for five days, and then 40 grains (2.59 Gm.) for an additional nine days. The total duration of treatment was fourteen days, and the total amount used, about 760 grains (48.88 Gm.).

DR. HARRY C. SAUNDERS: I should like to ask if patients with buboes which have broken down do as well as this patient has?

DR. HERMAN GOODMAN: Have any patients who failed to respond to therapy with antimony and potassium tartrate been given sulfanilamide?

DR. DAVID BLOOM: I am glad to hear of this effective treatment. If this drug is able to clear phagedenic chancroid in two weeks, great progress has been achieved in the treatment of this obstinate lesion. I hope that this beneficial effect will be confirmed by others.

DR. FRANK VERO: I should like to ask whether there has been any local treatment besides the administration of sulfanilamide?

DR. HERMAN GOODMAN: In the discussion will the presenter attempt to explain how a medicament supposed to be specific for cocci can benefit a disease caused by bacilli?

DR. BORRIS A. KORNBLITH (by invitation): As to the first question, about cases of buboes, inguinal enlargement was present in about two thirds of the cases. None of the lesions ever broke down. In 1 case a bubonulus formed on the shaft of the penis in addition to bilateral inguinal adenopathy. The whole picture at the onset was mistaken for lymphogranuloma venereum. Pus was aspirated from the bubonulus and treated in the same manner as Frei material. Cutaneous tests with this antigen yielded negative results in cases of lymphogranuloma and posi-

tive results in cases of chancroid. When the skin over the bubonulus broke down, it was possible to demonstrate the Ducrey bacillus without difficulty in the ulceration that remained. In other words, Ito-Reenstierna test material had been produced unwittingly. As to the use of antimony and potassium tartrate, I may present 3 cases in which the drug was given without any beneficial effect. In 1 case a condition that looked like chancroid clinically cleared up promptly during treatment with antimony and potassium tartrate, but it was never possible to demonstrate the Ducrey bacillus, and therefore, it could not be considered conclusively as Ducrey infection.

The only local therapy was cleansing with soap and water. I am aware, too, that in some cases the condition clears spontaneously with soap and water, but these patients were given the opportunity of clearing up the lesions by this method alone. If the lesions responded, sulfanilamide was not given. In the cases in which sulfanilamide was used there had been no response to the local therapy. The rationale of using sulfanilamide suggested itself from the effectiveness of the drug against streptococcic and bacillary infections. Therefore, I thought the Ducrey bacillus, a streptobacillus, might yield to this drug. It is amazing that the results have been so good. I did not expect them to be, even in only 24 cases. In contrast with my work with gonorrhea, in which I found results in only 45 per cent of cases, with chancroid I had over 95 per cent good results. There is one more point I want to mention: In the last group of 10 cases I used sulfanilamide powder in addition to oral treatment. I found local application of the powder does not alter the time of recovery. That is, the action of the drug is probably systemic and not local.

DR. E. WILLIAM ABRAMOWITZ: Have there been any reactions to the drug in cases of chancroid?

DR. HERMAN GOODMAN: What was the proportion of white to Negro patients treated with sulfanilamide?

DR. BORRIS A. KORNBLITH (by invitation): I can answer Dr. Abramowitz' question now, from the number of cases already observed. About 170 patients have been treated with sulfanilamide, with a dose as high as 140 grains (9.1 Gm.) per day. There were alarming symptoms in only 1 or 2 cases, in which the symptoms subsided in about twenty-four hours. All the patients have been ambulatory. They all had the usual mild symptoms—that is, moderate cyanosis, drowsiness and some change in mental acuity. Otherwise, the general symptoms from sulfanilamide in the dose given were negligible.

The group consisted of about one-half white and one-half Negro patients. The good and poor results were similar in the two groups. There were no cases of agranulocytosis.

DR. LOUIS CHARGIN: It is remarkable how few of the patients have had a rash.

DR. BORRIS A. KORNBLITH (by invitation): There were 3 cases of eruption due to sulfanilamide. The statement is sometimes made that when patients get an eruption their disease is likely to clear up. That did happen in 2 cases. A patient had received only 100 grains (6.5 Gm.) of sulfanilamide for gonorrhea when a rash developed; the disease cleared up in thirty-six hours. He had no other treatment. On the other hand, another patient had taken approximately 480 grains (31.1 Gm.) when a rash developed, but the disease continued unchecked.

Lymphogranuloma Venereum. Presented by DR. HARRY C. SAUNDERS.

L. D., a Negress aged 25, presented from the Bellevue Hospital, states that four years ago she noticed a nodular mass on the left shoulder, which broke down. A similar lesion developed on the forehead and another on the upper, inner part of the thigh. The Wassermann reaction was 4 plus, and she was given three intravenous injections. Last year she received two more intravenous injections. She has had a purulent vaginal discharge for two years. Six months ago she

noticed swelling of the vulva. She has been constipated and has had a bloody purulent discharge for two months. There has never been any inguinal swelling.

Proctoscopic examination showed beginning stricture and ulceration of the rectal mucosa. A barium enema showed rectal stricture. The Frei test with antigen prepared from the pus of mice and of human beings gave positive results. On March 1, 1938, the Wassermann reaction was 4 plus; examination of the spinal fluid gave negative results, and smears for gonorrhea gave positive results.

MINNESOTA DERMATOLOGICAL SOCIETY

LOUIS A. BRUNSTING, M.D., *President*

St. Paul, Feb. 4, 1938

F. W. LYNCH, M.D., *Secretary*

A Case for Diagnosis (Erythema ab Igne?). Presented by DR. JOHN F. MADDEN, St. Paul.

M. S., a girl aged 16, has congenital scoliosis with paraplegia and essential epilepsy. The nurse noticed a retiform erythematous macular eruption on the midportion of the back on Nov. 1, 1937. The patient states that the eruption appeared suddenly and that neither heat nor local medication had been applied. She had been getting phenobarbital at the time, but she had been taking this drug previously for eighteen months. The eruption is retiform, macular and deep brown.

A histologic section was shown.

DISCUSSION

DR. CARL LAYMON, Minneapolis: This case might possibly be one of post-inflammatory melanosis, in view of the fact that there is a history not of the application of heat but of an erythematous eruption following medication. The localization, however, does not fit such a diagnosis. Clinically the pigmentation is not unlike that following lichen planus.

DR. JOHN F. MADDEN, St. Paul: The girl had been taking phenobarbital for eighteen months before the eruption appeared and has been taking it constantly to date.

DR. LOUIS A. BRUNSTING, Rochester: My first impression was of tinea versicolor in the presence of Pott's disease and hyperhidrosis. However, scaling and definitely pigmented maculopapules were absent. The rare condition known as achromia parasitaria should be considered.

Gangrenous Pyoderma Accompanied with Hemorrhagic Colitis. Presented by DR. JOHN F. MADDEN, St. Paul.

I. M. L., a girl aged 8 years, has been ill since the fall of 1935, when she had bloody stools and indefinite discomfort and pain in the abdomen. A diagnosis of appendicitis was made, and an appendectomy was performed. In January 1936 she became listless, with fever and loss of appetite, and appeared weak. She had edema of the right knee, hemorrhages in the scleras and edema of the eyelids. The illness lasted the greater part of 1936. In January 1937 the symptoms recurred, accompanied with bloody stools, and the temperature rose to 103 F. In February 1937 abscesses appeared on the skin of the extremities, the face and the scalp. The abscesses drained spontaneously; sinuses formed, and the old lesions healed while new ones appeared. Some of the abscesses formed ulcers of irregular outline, which spread peripherally, and a verrucous border of pinhead-

sized pustules developed. Several ulcers were found on the scalp, the extremities and the face. At this time the patient was having from ten to twenty bloody stools a day and was rapidly losing weight.

Roentgenograms of the radius and the ulna showed new bone formation and periostitis. The Wassermann reaction was negative. Examination of the urine and of the blood showed no abnormality. The Mantoux test gave a slightly positive result. Repeated blood cultures showed no growth. The sugar content of the blood was 133 mg. per hundred cubic centimeters. Blastomycetes could not be found in the pus, on culture or on histologic examination.

Histologic sections were shown.

DISCUSSION

DR. L. H. WINER, Minneapolis: I was much more impressed by the microscopic section than by the clinical picture. The earlier section showed multilocular vesiculation and an infiltrate of giant and epithelioid cells. The later section showed a deep round cell infiltrate.

DR. LOUIS A. BRUNSTING, Rochester: The clinical picture and the microscopic sections are perfectly compatible with the various stages of this condition in cases that I have observed. On the one hand, there is abscess formation with liquefaction necrosis and, on the other, vegetative proliferation and a foreign body reaction, with all the stages between these two at different times.

Ulcerative colitis in a child of this age has a serious prognosis. Surgical resection of the bowel is attended with a prohibitive operative risk, and even in case of survival there is no assurance that the process will not involve other parts of the bowel. In medical treatment attention to the general health should be emphasized, a diet high in calories and vitamins prescribed and repeated transfusion of small amounts of blood and cautious administration of arsenic by mouth practiced.

Erythema Nodosum. Presented by DR. JOHN F. MADDEN, St. Paul.

W. F., a married woman aged 28, states that olive-sized painful erythematous nodules appeared on the anterior surfaces of the legs on Jan. 4, 1938. In 1933 the patient had a persistent cough, and coarse rales were heard in the bases of both lungs.

Roentgenograms showed increased prominence of the shadow of the root and of the basal markings of the right lung. Two roentgenograms taken in 1935 showed no change. A Mantoux test in 1937 gave a strongly positive result. This test caused pain and edema of the right forearm, which did not subside for about ten days. The sputum repeatedly showed no tubercle bacilli. The Wassermann reaction was negative.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I think the members are all agreed that every patient with erythema nodosum deserves a careful examination for possible cause. In my cases I have rarely been able to demonstrate tuberculosis, but I am sure the members are all aware that in the literature this etiology is being constantly discussed.

DR. LOUIS A. BRUNSTING, Rochester: This condition so frequently is associated with acute infection of the tonsils and the teeth that I have come to assume that it is a reaction to a streptococcus, not necessarily of hemolytic type. In several instances in which sulfanilamide has been used there has been no appreciable benefit.

A Case for Diagnosis (Lichen Ruber Moniliformis? Lichen Planus?). Presented by DR. JOHN F. MADDEN, St. Paul.

This case was presented at the last meeting of the Minnesota Dermatological Society (ARCH. DERMAT. & SYPH. **37**:725 [April] 1938), and subsequent findings are given. There are four distinct types of lesions. Heavy infiltrated brownish

red plaques covered with a yellow greasy scale are present in the eyebrows, around the mouth and on the cheeks. Discrete pea-sized slightly erythematous superficial papules covered with a greasy fine scale appear on the trunk. Discrete and connected longitudinal lines made up of pinhead-sized annular violaceous papules and a slight scale are present on the flexor surfaces of the arms and the forearms, being most marked in the antecubital spaces. Similar lesions are present to a lesser extent on the extensor surfaces of the knees. The soles are covered with punctate pinhead-sized discrete and confluent keratoses. The eruption first appeared in the antecubital spaces in 1929 as small red papules.

The lesions on the arms have been present since 1933. There are no subjective sensations. None of the lesions have disappeared. In 1933 small erythematous papules appeared on the upper lip. The lesions on the face almost disappeared in the summer and became worse each winter. The lesions have been present on the feet since 1933 and on the trunk since 1935. The eruption was markedly aggravated during a recently terminated pregnancy. The baby was born at term and was normal in every respect. Many ointments used locally have produced no improvement.

A blood count showed 60 per cent hemoglobin, 7,600 leukocytes, 3,070,000 erythrocytes, 64 per cent polymorphonuclears and 36 per cent lymphocytes. The calcium content of the blood was 8.6 mg. per hundred cubic centimeters and the urea nitrogen content 15.4 mg. The Wassermann reaction was negative, and the icterus index was 12.

Histologic sections from lesions on the shoulder, the flexor surface of the arm, the eyebrow and the foot were shown.

DISCUSSION

DR. STEPHAN EPSTEIN, Marshfield, Wis. (associate member): The section from the arm shows a structure resembling lichen planus. The picture of the other sections is not specific. Psoriasis may be excluded microscopically. I think the condition may be atypical lichen planus.

DR. L. H. WINER, Minneapolis: Microscopic section showed nothing specific. Microscopic section in the case of Fred Wise and C. R. Rein (ARCH. DERMAT. & SYPH. **34**:830 [Nov.] 1936) showed an increase in the connective tissue in the involved areas, which were papules, whereas microscopic section in this case showed a predominance of round cell infiltrate.

DR. CARL LAYMON, Minneapolis: I think that dermatologists throughout the years have been grouping lichen ruber moniliformis in some cases with lichen planus. In fact, the disease has been described in several textbooks, as a part of lichen planus. The chief differences between this case and other cases previously reported is that the lesions assume a less keloidal aspect in the cubital spaces.

DR. H. E. MICHELSON, Minneapolis: I think before any great discussion on this condition is undertaken a definition should be decided on. I think that Dr. Madden must show that lichen ruber moniliformis is a disease by itself and must prove or disprove its association with or membership in psoriasis or lichen planus.

DR. JOHN F. MADDEN, St. Paul: Some parts of this eruption resembled lichen planus, psoriasis, seborrheic eczema and chronic lupus erythematosus. The diagnosis of lichen ruber moniliformis was considered because of the moniliform character of the eruption, the nonspecific histologic picture, the asymptomatic nature of the eruption and the lack of response to treatment for years.

Lupus Erythematosus. Presented by DR. JOHN F. MADDEN, St. Paul.

V. E. H., a married woman aged 39, has had a recurrent eruption on the face, the chest, the abdomen and the legs since 1920. The lesions remain about three months and disappear without scarring. The new lesions are tender on palpation. The eruption consists of slightly erythematous papules varying in size from that of a pea to that of a dime, with dilated follicular orifices and slightly

adherent scale. The patient has had contact with 3 persons who died of pulmonary tuberculosis. In 1927 she went on a reducing diet, and a chronic cough developed.

The sputum showed many tubercle bacilli, and a diagnosis of pulmonary tuberculosis was made. The Mantoux test gave a strongly positive result. She spent eighteen months in 1927 and 1928 in a sanatorium because of advanced pulmonary tuberculosis with cavitation. A roentgenogram taken in January 1938 showed normal lungs. The Wassermann reaction was negative.

Histologic sections from lesions on the cheek, the chest and the arm were shown.

DISCUSSION

DR. CARL LAYMON, Minneapolis: In his last writings Kren was still emphatic as to the tuberculous etiology of lupus erythematosus. He stated that he found definite evidences of tuberculosis in an extremely high percentage of cases. He stressed the eye as a frequent focus of tuberculosis.

DR. STEPHAN EPSTEIN, Marshfield, Wis. (associate member): The clinical picture is not typical at present. There are hard nodules on both elbows which showed deep infiltrations microscopically. I am not sure that I saw little nests of epithelioid cells. I think the condition might be an atypical tuberculid.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: There are no signs of scars at the sites usually involved by disseminated lupus erythematosus. If this woman had had such a condition for ten years, I should expect more constitutional reaction and debility. Like Dr. Epstein, I think that the lesions at present are atypical tuberculids.

DR. JOHN F. MADDEN, St. Paul: The eruption has changed since the patient was first seen. The histologic section from the lesion on the cheek was in keeping with the diagnosis of lupus erythematosus. There are none of the characteristics of dermatitis herpetiformis, such as grouping, hyperpigmentation, scaling and extreme pruritus. I agree with Dr. Epstein that the condition may be some type of tuberculid.

Chronic Inflammation in Tattoo Mark. Presented by DR. JOHN F. MADDEN, St. Paul.

J. A., a man aged 27, was tattooed on the flexor surface of the left arm in July 1930. Immediately the entire tattooed areas became raised, inflamed and slightly painful. The portion that was tattooed red remained elevated, inflamed and painful, but the blue part of the tattoo subsided to the level of the surrounding normal skin within three weeks. After this the pain disappeared, but the red areas of tattoo remained elevated, scaly and slightly pruritic.

A Mantoux test gave a negative result. The Wassermann reaction was repeatedly negative. Roentgenograms showed an accentuation of the markings in the upper lobe of the right lung, suggesting fibrosis.

The histologic section showed a chronic inflammatory reaction in the areas of red tattooing.

DISCUSSION

DR. L. H. WINER, Minneapolis: Two cases of similar type have been reported, 1 by P. Unna (*Arch. f. Dermat. u. Syph.* **160**:153, 1930) and 1 by D. B. Ballin (ARCH. DERMAT. & SYPH. **27**:292 [Feb.] 1933). Unna's patient, a man aged 73, had been tattooed in his youth. At the age of 43 he contracted syphilis and received antisyphilitic therapy. Unna thought the reaction in the tattoo was due to sensitization to mercury. A patch test with mercury gave a positive result. Ballin's patient, a man aged 20, had the lesion in the tattoo for two years. Again only the red areas were involved. A patch test with 2 per cent ammoniated mercury gave a positive result. There had been no previous mercurial therapy in this case. Both patients had negative reactions to patch tests with cinnabar. Microscopic sections showed a nonspecific inflammatory process in the cases reported. It is interesting that members of the Strasbourg

school in two papers, by J. Lacassagne and J. Rousset (*Bull. Soc. franç. de dermat. et syph.* **38**:919, 1931) and by L. M. Pautrier, F. Woringer and Esquier (ibid. **39**:310, 1932) discussed the frequency of keloid in tattoo. They rarely found true keloid in tattoo.

DR. JOHN F. MADDEN, St. Paul: Dr. Belote, of the University of Michigan, showed that the lesions of syphilis did not appear in the red (cinnabar) portion of a tattoo, while they did appear in the blue portion.

A Case for Diagnosis (Borderline Erythema Nodosum? Erythema Multiforme?). Presented by DR. JOHN F. MADDEN, St. Paul.

Purpura Associated with Arthritis. Presented by DR. JOHN F. MADDEN, St. Paul.

A Case for Diagnosis (Pruritus and Dermatitis Accompanying Cirrhosis of the Liver?). Presented by DR. JOHN F. MADDEN, St. Paul.

Recklinghausen's Disease. Presented by DR. JOHN F. MADDEN, St. Paul.

Acne Varioliformis. Presented by DR. JOHN F. MADDEN, St. Paul.

Generalized Vaccinia. Presented by DR. JOHN F. MADDEN, St. Paul.

Neurotic Excoriations; Acarophobia. Presented by DR. JOHN F. MADDEN, St. Paul.

Granuloma Annulare. Presented by DR. JOHN F. MADDEN, St. Paul.

A Case for Diagnosis (Dermatitis Herpetiformis; Pyoderma). Presented by DR. JOHN F. MADDEN, St. Paul.

A Case for Diagnosis (Dermatitis Due to Bismuth?). Presented by DR. JOHN F. MADDEN, St. Paul.

Epidermolysis Bullosa (Report on a Case Previously Presented). By DR. H. E. MICHELSON, Minneapolis.

A Case for Diagnosis (Disturbance of Growth of Nails). Presented by DR. H. E. MICHELSON, Minneapolis.

LOS ANGELES DERMATOLOGICAL SOCIETY

THOMAS W. NISBET, M.D., *Chairman*

Feb. 8, 1938

CHARLES W. CASKEY, M.D., *Secretary*

A Case for Diagnosis (Healed Scleroderma?). Presented by DR. SAUL S. ROBINSON.

P. S., a white American woman aged 30, has a fairly well defined brownish pigmented atrophic plaque with islands of depigmentation on the anterior surface of her left thigh. There are similar but smaller areas on the back of the left thigh. Serologic tests were negative. Previous treatment has consisted of a few roentgen treatments and administration of thyroid. No improvement has been noted.

DISCUSSION

DR. SAMUEL AYRES JR.: I cannot see any evidence of scleroderma. The patient states that there has been no infiltration. I should consider the condition idiopathic atrophy.

DR. KENDAL FROST: Not only was the skin involved but there was definite muscular atrophy. The mechanism here is similar to that seen in hemiatrophy of the face. The injury was probably succeeded by scleroderma and then atrophy. The microscopic picture included a peculiar ballooning of the rete cells, for which I cannot account.

The microscopic picture had some features that might fit in with poikiloderma of Jacobi, but the clinical appearance certainly does not, at least not with the type that Jacobi originally described and to which I still restrict the term. Oppenheim has included a larger group under this heading. Even if this picture can be included in the larger group, I think injury to a nerve with peculiar resulting behavior is the mechanism.

DR. H. C. L. LINDSAY: I think the injury is a factor in this case. Atrophic disturbance of a nerve could produce pigmentation with the atrophy. In this case the injury appears to have been the beginning of the neural atrophy which preceded the cutaneous atrophy.

DR. H. S. CAMPBELL: This patient came to the Good Hope Clinic. Dr. Robinson thought the manifestation an atrophic aftermath of scleroderma, while I believe it to be poikiloderma atrophicans vasculare of Jacobi. The case is presented for diagnosis.

The most conspicuous feature in the section is that in the rete layer spongiosis is present, while the cells themselves show vacuolation and granular changes in the protoplasm. The nuclei, many of them sickle shaped, are pushed over to the walls of the cells. Vascular proliferation is especially marked in the papillary layer. Some of these changes are characteristic of those found in Jacobi's poikiloderma. The corium gives no indication of hypertrophy of the collagenous tissue or of the changes in the vessel walls that remain as an aftermath of scleroderma.

Blue Nevus (Face); "Mongolian Spots" (Sacrum). Presented by DR. SAMUEL AYRES JR.

B. O., a Japanese girl aged 1 year, has an oval greenish blue macule half the size of a dime in the right cheek and two slate gray macules of about the same size in the lumbosacral region. These have been present since birth. She has typical mongolian blue spots on the sacrum, and the question is whether the lesion on the face belongs in the same category. The parents are much concerned about the facial lesion, because the patient is a girl. The blue coloring is attributable to the fact that the brown granules of melanin are deep seated and separated from the surface by nonpigmented cells. The patient is presented for therapeutic suggestions.

DISCUSSION

DR. F. I. BALL: The melanotic lesions are probably of the mongolian blue spot type.

DR. KENDAL FROST: I believe all these lesions are identical and are probably mongolian spots. A histologic examination of one of the sacral lesions would settle the question, and treatment of the lesion on the face would depend on the diagnosis established by that procedure.

DR. H. S. CAMPBELL: The few blue nevi I have seen have been much smaller than this particular one. While both the nevus and the mongolian spot are examples of mesenchymal melanoblasts, the pigment cells are much more numerous in the former. Usually in the latter the cutis shows only large single stellate cells here and there. Under the circumstances, I believe that if the parents want

the lesion taken off it would be justifiable to consider it as a lesion possessing potential melanosarcomatous degenerative properties. In this way the potentiality would be removed and its exact nature determined.

DR. SAMUEL AYRES JR.: Textbooks are sketchy in their description of mongolian blue spots. The statement is generally made that they disappear when the patient is about 2 or 3 years old. In a case like this, a scar will follow removal of the lesion, and if there is a chance of its disappearing spontaneously one would not like to remove it and leave a scar. The cosmetic effect is important in this case. M. Tièche (*Virchows Arch. f. path. Anat.* **186**:212, 1906) described a number of cases of blue nevus and expressed the belief that in a certain number of them the growth was potentially malignant.

Coccidioidal Granuloma. Presented by DR. HARRY P. JACOBSON.

J. R., a Filipino aged 24, came to my service at the Los Angeles County Hospital in May 1937, at which time he was acutely ill with systemic and cutaneous coccidioidal granuloma. The cutaneous lesions consisted of ulcerating nodules, fistulas, abscesses and flaccid tumor-like growths. For a long time he was in a septic condition. Treatment with vaccine and halibut liver oil and rest have produced a satisfactory response.

DISCUSSION

DR. KATHERINE MACEACHERN, Los Angeles (by invitation): The most striking thing about this case is the effect of intravenous therapy. The patient had been receiving increasing doses of coccidioidal vaccine intramuscularly. The course was slow, and there was little visible effect. About eight months ago Dr. Jacobson decided to try injecting the vaccine intravenously, and after two injections the patient was able to leave the hospital. His reactions consisted of severe headache and malaise for forty-eight hours following the intravenous injections.

DR. H. S. CAMPBELL: I would not speak of the specific or nonspecific reaction but of the differences that obtain between intramuscular and intravenous injection. Continental students often refer to Kyrle's experiment in a case of old nodular leprosy, in which a subcutaneous pustule was produced by local injection of a chemical irritant. The aspirated matter was dissolved in saline solution and used intravenously, and chills and attacks of exceedingly high temperature followed. These attacks were followed by resolution of most of the nodules. After the second injection the nodules disappeared, and the patient was apparently cured. In a later case the first injection gave much the same profound reaction, but the later injections proved inert. At a later date I utilized both a similar solution and extracts of nodular tissue intramuscularly, with but mediocre results. No fever or other reaction was obtained. I would contend that intravenous therapy differs markedly from intramuscular therapy, both in the reaction and in the results obtained.

DR. WILLIAM H. GOECKERMAN: There is no doubt in my mind that there is a difference between intramuscular and intravenous injections of the same substance, dependent not on the size of the dose alone but on the biologic features involved.

DR. SAMUEL AYRES JR.: I have used the intravenous route exclusively in administering vaccines for five or six years. Much work has been done by investigators in arthritis, who state that better immunization and much less chance of sensitization accompany intravenous than subcutaneous therapy. I have had success in cases of furunculosis, particularly those in which there have been recurring attacks following subcutaneous injections of vaccine. Apparently a much higher degree of immunity has been established than on previous occasions when the patients have had subcutaneous injections. I think Dr. Jacobson has contributed something of value. It is possible that part of the benefit is due to the size of the dose, which is large enough to cause a systemic reaction.

DR. HARRY P. JACOBSON: When the patient came to the Los Angeles County Hospital, the prognosis appeared poor. After a certain degree of improvement from subcutaneous and intramuscular administration of coccidioidal vaccines, his condition became stationary. I then began to administer the vaccine intravenously, and the therapeutic results were fairly spectacular. I might say that I have had a similar experience in a number of other cases in the past year or so. In the average case coccidioidal granuloma will respond to cutaneous, subcutaneous or intramuscular injection of vaccine up to a certain point and then remain stationary. A change to the intravenous route will then accelerate the progress and bring about further improvement. I cannot agree with Dr. Goeckerman that the benefit from coccidioidal vaccine should be ascribed to a nonspecific immunity response to the protein factors contained in the antigen. I believe the reaction is specific. However, I shall ask Dr. Goeckerman to give typhoid vaccine intravenously to the next patient with coccidioidal granuloma who comes to the service and to observe results.

The initial dose, 0.05 cc., is increased by 0.05 cc. at each successive injection unless contraindications develop. The reaction is local, focal and systemic. The patient frequently has chills and a rise in temperature several hours after the injection, and a tolerance to the same or a smaller dose seems to develop.

Extensive Psoriasis. Presented by DR. HARRY P. JACOBSON.

J. B., a white man aged 40, states that an eruption began twelve years ago on the dorsum of the right hand. At present it is generalized, involving the entire skin except the palms. The eruption on the trunk and the extremities is made up of variously sized and shaped flat irregular macule-like elements. The color varies from pink to deep red. The lesions are closely aggregated and in many places are confluent to form large patches. There is generalized dry silvery scaling, and the removal of scales reveals the characteristic papillary bleeding points. The plantar surfaces are hyperkeratotic and dry. The interdigital spaces show evidence of maceration and peeling. The nails do not show any dystrophy, except those of the thumbs, which show transverse grooving and thickening of the proximal halves. In the scalp are diffuse scaling patches.

Chemical examination of the blood showed no abnormality, and serologic tests were negative. A test of the urine for arsenic showed 0.00025 mg. per hundred cubic centimeters. Spectroscopic analysis of tissue (by weight) showed aluminum 0.01, barium from 0.001 to 0.01, boron 0.001, copper 0.01, iron 1, lead from 0.001 to 0.01, magnesium 1, nickel 0.001, potassium from 0.01 to 0.1, silicon from 0.01 to 0.1, silver from 0.0001 to 0.001 and sodium from 0.1 to 1 per cent.

A histologic study revealed irregular acanthosis and thinning of the epidermal layers and some hyperkeratosis. The granular layer was absent in some places and consisted of only one layer of cells in others. There was a fairly marked cellular infiltrate of the papillary and the subpapillary zone of the cutis.

The patient has been given halibut liver oil with viosterol in increasing doses and injections of ascorbic acid.

DISCUSSION

DR. WILLIAM H. GOECKERMAN: If I can base my diagnosis on the picture present tonight I shall unhesitatingly call this condition parapsoriasis of the type of parakeratosis variegata.

DR. H. S. CAMPBELL: I believe this case to be one of parapsoriasis both because of the clinical picture and because of the difficulty of believing that psoriasis would persist in a patient for twelve years without more marked fluctuation. The chronicity alone would indicate parapsoriasis.

DR. SAMUEL AYRES JR.: I think the condition is parapsoriasis. The facts that the lesions began on the backs of the hands and gradually developed elsewhere, that the nails are entirely free from involvement and that the lesions are diffuse would all speak against psoriasis. Whether the patient's having worked

in copper mines has introduced any element of metallic poisoning I do not know. I should not regard this condition as real psoriasis.

DR. NELSON PAUL ANDERSON: This case belongs in the same group as those of dermatophytosis presented by Dr. Ayres Dec. 14, 1937 (ARCH. DERMAT. & SYPH. **37**:1066 [June] 1938). Many of the members thought that those were cases of psoriasis. The patient states that this condition started while he was working for the American Can Company, and he credits the involvement of his right toe nails to an injury at that time, which might have precipitated the infection. Dr. Jacobson is to be congratulated on presenting this case. There are involvement of the toe nails of one foot and annular ringworm lesions on the body. Dr. Jacobson states that the patient gave a tremendous reaction to trichophytin. It is uncommon for patients with this disease to give such a reaction. Most of them fail to give any reaction to either stock or autogenous trichophytin. I think this case belongs in the same category as the 2 cases presented at the last meeting, namely, with cases of infection by T. purpureum. This whole subject has been carefully and thoroughly investigated, and much new knowledge has been contributed through the splendid work of Dr. George M. Lewis of New York.

DR. HARRY P. JACOBSON: Dr. Anderson's reference to cutaneous reactions to trichophytin is pertinent to the present discussion. This patient presents two definite types of lesion: (1) a superficial, desquamating eruption consisting of variously sized and shaped plaques devoid of inflammatory reaction and (2) a markedly inflammatory reaction consisting of nodular elements arranged in circinate patches with serpiginous borders. The same organism was recovered from the scales of both types of lesions. The cutaneous reaction to the fungus antigen injected in this case I believe should be interpreted as an immunologic reaction and not a response due to sensitization. I consider this reaction to be predicated on the same biologic responses as are the nodular lesions themselves, viz., response of the tissue to a biologic insult. It is possible that if this patient's skin had been incapable of responding with inflammatory lesions of nodular or other type he would not have responded with an inflammatory reaction in situ to injection of a fungus antigen.

DR. SAMUEL AYRES JR.: I should like to ask Dr. Jacobson what he means by immunologic reaction? Desensitization and immunization are two different processes, the former being possible without the latter. I prefer the terms immune reaction and desensitization reaction.

DR. HARRY P. JACOBSON: There is fluctuation in the cutaneous eruption. It is distinctly worse in the cold winter months and improves in the summer months. The patient complains of an unusual degree of pruritus. The microscopic architecture of the sections of tissue is certainly consistent with the diagnosis of psoriasis. I have considered all the diagnostic possibilities enumerated tonight, and I still believe that this patient has psoriasis of an unusually extensive distribution.

SAN FRANCISCO AND LOS ANGELES DERMATOLOGICAL SOCIETIES

N. N. EPSTEIN, M.D., San Francisco, *Chairman*

Joint Meeting, San Francisco, Feb. 12, 1938

H. V. ALLINGTON, M.D., Oakland, Calif., *Acting Secretary*

Pemphigus Vulgaris. Presented by DR. H. J. TEMPLETON, Oakland, Calif.

J. L., an American-born Jew aged 43, noted soreness in his mouth about one year ago. This was tentatively regarded by his physician as trench mouth. About

six months ago a lesion appeared over the left pectoral region, which was regarded as a local infection. It still persists.

About two months ago the patient was given three injections of 0.6 Gm. of neoarsphenamine and about 100 tablets of sulfanilamide for the oral and cutaneous lesions. The administration of the neoarsphenamine was followed by chills and a temperature of 104 F., which disappeared in three or four days. Shortly afterward "blisters" appeared on his hands and feet.

The patient's general health has always been excellent. Complete physical examinations by two internists disclosed nothing noteworthy except two abscessed teeth, which have been extracted recently. Streptococcus viridans was cultured from the pulp of the extracted teeth. Other laboratory tests showed nothing noteworthy.

A course of fever treatments induced by typhoid-paratyphoid vaccine intravenously produced no improvement. At present he is receiving tryparsamide and a blood coagulant (coagulen) on alternate days. Two weeks of this treatment have not altered the picture. He is also being given heavy doses of the various vitamins empirically.

The case is presented for suggestions as to further therapy; I have germanin therapy particularly in mind.

DISCUSSION

Dr. Samuel Ayres Jr., Los Angeles: I should like to ask whether any of the members has used massive doses of viosterol, as recommended by J. B. Ludy and C. M. DeValin (*Urol. & Cutan. Rev.* **36**:817 [Dec.] 1932). Several years ago I had a patient with the Senear-Usher type of pemphigus which developed into the bullous type. The condition improved during administration of massive doses of viosterol together with intravenous injections of sodium gold thiosulfate.

Dr. H. J. Templeton, Oakland, Calif.: This patient has been receiving 200,000 units of viosterol daily for at least two weeks, and there has been no improvement. My last patient with this disease, who died, had this same treatment with no improvement.

Dr. Harry E. Alderson, San Francisco: I hesitate to relate my experience with just 1 case of pemphigus treated with germanin. The patient, a woman, received two courses of germanin, which apparently had no effect; she died.

Dr. L. F. X. Wilhelm, Los Angeles: I used germanin in 1 case and did not see any effect from it.

Pemphigus. Presented by Dr. F. G. Novy Jr., Oakland, Calif.

M. L. C., a Jew aged 50, was first seen in the University of California dermatologic clinic on Dec. 6, 1937. At that time he stated that for several months he had had a sore mouth and throat with swollen glands in the neck, burning of the eyes with lacrimation and purulent discharge, general malaise, loss of weight and slight elevation of temperature. One week before entry, solitary blisters appeared on the chest, the back and the arms, each lasting a few days. Scattered new ones appeared daily. At present these lesions are vesicular and show a tendency to grouping on the chest, the lower part of the abdomen and the central part of the back. There are pigmented stains of old lesions. The conjunctivas are red and injected. The throat shows symmetric superficial ulceration. The gums and buccal mucosa show many shallow ulcers covered with a grayish white membrane. Physical examination showed no other significant findings.

A blood count and urinalysis showed no abnormality. Smears from the lesions in the throat and mouth showed no specific bacteriologic picture.

DISCUSSION

Dr. H. E. Miller, San Francisco: This case is of interest because the patient had the oral lesions for approximately four months before lesions appeared else-

where on the body. The lesions in the mouth were superficially ulcerated, and lichen planus and a monilial infection were considered in the differential diagnosis. Only when bullae developed on his body was the diagnosis of pemphigus definitely established.

DR. L. R. TAUSSIG, San Francisco: The suggestion has been made in the European literature that sulfanilamide be given. The logic of such medication is not clear, but a few cases have been reported in which the result was favorable.

DR. SAMUEL AYRES JR., Los Angeles: No benefit resulted from adequate dosage of sulfanilamide for one week in 1 of my patients with pemphigus.

DR. N. N. EPSTEIN, San Francisco: The patient shown today by Dr. Templeton had sulfanilamide but there was no improvement.

NOTE.—Both Dr. Novy's and Dr. Templeton's patient died about a month after presentation.

Dermatitis Herpetiformis. Presented by DR. J. M. GRAVES, San Francisco.

S. G., an Italian man aged 63, was first seen at the University of California dermatologic clinic on March 22, 1936. At that time he presented a generalized eruption of nine months' duration. On the feet, particularly on the dorsal aspects, the eruption consisted of erythematous patches, papules, vesicles and pustules, with considerable crusting of many of the lesions. On the rest of the body the eruption consisted mainly of confluent patches of erythema with crusting and excoriations. Eight years before he had had a similar rash, which began around the ankles and spread upward to involve the whole body with the exception of the face.

Physical examination gave essentially negative results.

Local treatment consisted of daily baths with starch and soda and application of compresses of 0.5 per cent aluminum acetate. Solution of potassium arsenite was given by mouth. There was gradual improvement. In six months the skin was clear, and all treatment was discontinued. On Jan. 22, 1938, he was again seen in the clinic, because of a recurrence of the eruption over the trunk and the arms of one month's duration. The treatment previously used was again instituted.

A blood count on March 22, 1936, revealed 78 per cent hemoglobin, 4,000,000 erythrocytes and 20,400 leukocytes. A differential count showed 72 per cent polymorphonuclear neutrophils, 12 per cent eosinophils, 2 per cent basophils, 4 per cent lymphocytes and 10 per cent monocytes. On Jan. 22, 1938, the count showed 88 per cent hemoglobin, 4,390,000 erythrocytes and 8,480 leukocytes, with 69 per cent polymorphonuclear neutrophils, 6 per cent eosinophils, 19 per cent lymphocytes and 6 per cent monocytes.

A patch test with sodium iodide in March 1936 gave negative results.

Sections of tissue from the skin of the arm and of the abdomen showed histologic changes characteristic of dermatitis herpetiformis.

DISCUSSION

DR. STANLEY CHAMBERS, Los Angeles: The clinical characteristics did not impress me as those of dermatitis herpetiformis. The multiform characteristics of this disease are well appreciated, and it may well be that the present picture is only a phase of the disease. I should be more impressed with the possibility of disseminate neurodermatitis.

DR. WILLIAM H. GOECKERMAN, Los Angeles: I feel that disseminated neurodermatitis and toxic dermatitis should be carefully considered in this case.

DR. MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif.: What may be seen today does not substantiate the diagnosis of dermatitis herpetiformis. I believe that a diagnosis of contact dermatitis due to irritation from a strong soap used in washing his underwear should be considered.

DR. KENDAL FROST, Los Angeles: I agree with the diagnosis as presented. Dermatitis herpetiformis may present protean manifestations, and thus those who are able to observe a case over a long period are much more able than others to arrive at a diagnosis. Characteristic vesicular lesions may be destroyed so quickly by scratching that they are never seen in their characteristic state. At times their presence is made known only by the description given by the patient.

DR. FRANCES TORREY, San Francisco: This patient at one time had many bullous lesions. He has had flare-ups and complete remissions without apparent changes in living habits (i. e., clothing, food and environment).

Neural Leprosy. Presented by DR. F. G. NOVY JR., Oakland, Calif.

F. J., a man aged 31, was presented at the meeting of the San Francisco Dermatological Society on Oct. 1, 1937 (ARCH. DERMAT. & SYPH. **37**:886 [May] 1938). Since then he has been taking increasing amounts of chaulmoogra oil. The dose at present is 200 drops three times a day. There appears to be some involution of the macules.

Neural Leprosy. Presented by DR. F. G. NOVY JR., Oakland, Calif.

M. P., a woman aged 25, was born in Mexico and at an early age moved to Brownsville, Texas, where she lived until she moved to Oakland, Calif., sixteen months ago. About one year ago she noticed some numbness on the right cheek; this was followed by considerable itching. A scaling patch then appeared in this area. Last spring similar lesions developed on the right shoulder, the medial aspect of the right foot and the medial surface of the left knee. These all started in the same way, with numbness, itching and then scaling of the skin. Since then, smaller areas have appeared elsewhere over the body. They all show increased pigmentation, which is more marked at the periphery, as well as scaling. The lesion on the cheek is erythematous. There is definite anesthesia in these areas. The peripheral nerves are slightly enlarged.

The Wassermann test was negative. Nasal smears on two occasions did not show acid-fast organisms. Sections of a specimen of skin taken from the shoulder are presented. They showed no acid-fast organisms. As yet a biopsy of nerve tissue has not been made.

Neural Leprosy. Presented by DR. HOWARD MORROW, San Francisco.

D. V., a Mexican woman aged 37, was first seen in the University of California dermatologic clinic in March 1934. She stated that sensation in both hands had been slight or absent for fourteen years. The absence of sensation was first observed at the time of a severe but painless second degree burn. Examination revealed ridged and deformed finger nails and toe nails. The terminal phalanges were atrophic; the skin was dry, and there was definite diminution of sensation over the fingers and toes. Otherwise the physical examination showed no essential abnormality except for cervical lymphadenitis. A node was aspirated and a biopsy performed. All cultures were negative, and no acid-fast organisms were observed. Microscopic examination of sections from the gland showed nonspecific granulation tissue. Roentgen therapy was given to the left cervical region.

In July 1934 the patient burned her left hand, and a nontender swelling developed on the left index finger. A roentgenogram showed considerable destruction of the distal half of the middle phalanx.

On Aug. 14, 1934, weekly intramuscular injections of 3 cc. of chaulmoogra oil were started. This medication was continued until May 31, 1937, with occasional periods of rest.

The condition improved somewhat, and in September 1937 the patient could vaguely distinguish between hot and cold but continued to burn herself frequently.

Frequently repeated nasal smears have shown no acid-fast organisms.

DISCUSSION OF CASES OF NEURAL LEPROSY

DR. STANLEY CHAMBERS, Los Angeles: It would be helpful if Dr. Morrow would explain the present attitude of public health officials in respect to this disease. I have always felt that physicians should assume absolute control or none at all. The fact that the disease is contagious, with accessible organisms to reproduce infection, does not seem to be completely outweighed by clinical observation of relatively infrequent transmission.

DR. HOWARD MORROW, San Francisco: The law states that when this diagnosis is made it must be reported and the patient isolated. Provision is made for this isolation and care at the United States Marine Hospital, Carville, La. Ordinarily the patients are isolated in the county hospitals until a group is gathered for transportation. However, there is no law to force a patient to go to Carville. For example, a man from Mount Diablo had leprosy but refused to go. Instead, he was isolated in his home until he finally died. A little while ago leprosy developed in his 15 year old son. The family was persuaded to take the boy to Carville.

Cushing's Syndrome (Basophilic Adenoma of the Pituitary Gland). Presented by DR. FRANCES TORREY, San Francisco.

N. J. H., a white woman aged 33, was first seen in the University of California Hospital on Dec. 12, 1937.

She had been normal and strong until she reached the age of 16, when she began to gain weight. Her trunk, face and neck especially became obese. She began to tire easily, and her arms and legs were extremely weak. The fat pads were extremely tender to touch and felt lumpy. Menstruation became scanty and finally ceased. Occasionally she had severe headache. There has been no hypertrichosis. Glycosuria has been present since the onset of her illness. Growth, except for the increase in fat, ceased. She is small and appears slightly older than her stated age. Her face is flushed, and the malar pads are puffy and prominent. She has an obese torso and neck and thin, flabby arms and legs. The skin is tender to the touch, dry and tense. There are symmetric dark brown pigmented areas over the legs, beginning abruptly at the ankles, spreading uniformly over the tibias and extending in a reticular pattern laterally to the calves. There are many irregular-shaped atrophic scars over the anterior portion of the pigmented areas.

The heart and lungs are normal. The blood pressure is 160 systolic and 100 diastolic. The genitalia are normal, and there is no evidence of ovarian tumor.

A blood count showed 120 per cent hemoglobin, 5,100,000 erythrocytes and 10,400 leukocytes, with 80 per cent polymorphonuclear neutrophils, 16 per cent lymphocytes, 2 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. Chemical study of the blood revealed normal amounts of proteins and of calcium and a slightly low (2.94 mg. per hundred cubic centimeters) phosphorus content. The Wassermann and the Kahn reaction were negative. A dextrose tolerance test revealed a mild diabetic curve. The sugar content of the blood during fasting was 143 mg. per hundred cubic centimeters. Roentgenograms of the long bones, the chest and the skull showed no abnormalities except widespread decalcification. The heart, the lungs and the sella turcica appeared normal. Pyelograms revealed a normal genitourinary tract. The visual fields were normal. The basal metabolic rate was —2 per cent.

The patient was placed on a special diet consisting of 160 Gm. of carbohydrate, 70 Gm. of protein and 100 Gm. of fat and given 15 units of insulin daily (5 units before breakfast and 10 units before dinner). The glycosuria was not controlled, and the patient did better on a regular diet low in sodium. Perirenal insufflation was not successful, but it was felt that roentgen treatment to the adrenal glands might benefit the patient. On Jan. 24, 1938, this was begun, and the patient received a total of 1,200 roentgens, divided into six daily doses of 200 r.

Cushing's Syndrome (Early). Presented by DR. FRANCES TORREY, San Francisco.

B. L., a white boy aged 16, was first seen in January 1938 in the University of California dermatologic clinic. He stated that obesity with mild hypertension began about five or six years ago.

He now complains of increasing weakness, malaise and headaches.

Physical examination shows a marked increase in the adipose tissue of the face, the trunk and the arms. There are symmetric purplish striae about the posterior axillary folds, on the arms and in the popliteal folds. There is a systolic murmur above the left pulmonic area. The blood pressure is 170 systolic and 100 diastolic.

Roentgen studies, including those of the sella turcica and the chest and pyelograms, showed no abnormality. The osseous age is 18 or 19.

Urinalysis showed no abnormality. A blood count showed 112 per cent hemoglobin, 5,300,000 erythrocytes and 6,970 leukocytes, with 33.2 per cent polymorphonuclear neutrophils, 12.6 per cent eosinophils, 0.6 per cent basophils, 49 per cent lymphocytes and 4.6 per cent monocytes. The Kahn and the Wassermann test were negative. The basal metabolic rate was + 11.5 per cent. Chemical examination of the blood showed the calcium content to be normal (10.93 mg. per hundred cubic centimeters) and the phosphorus content slightly low (2.82 mg.); the chloride content of the plasma was 589 mg. per hundred cubic centimeters. A dextrose tolerance test showed, during fasting, 95 mg., and at one hour and at five hours after ingestion of food, 200 mg. and 81 mg., respectively, per hundred cubic centimeters.

DR. FRANCES TORREY, San Francisco: All 3 patients have the same physical

M. B., a man aged 20, a farmer, was first seen in the University of California Hospital on Dec. 13, 1937.

He was well until he reached the age of 15, when arthritis developed in the right elbow and the left knee. After this he began to have headaches and pain in the back, both of which were more severe at night, when he was lying down. His blood pressure at that time was elevated (170 systolic), and he was gaining weight without increasing in stature. Rather marked hypertrichosis developed, but his voice never changed. Polyuria has been present since the onset of his present illness.

Examination reveals a short man with thin extremities and marked obesity of the trunk, especially around the shoulders, the chest, the neck and the upper part of the back. The trunk is covered with fine black hair, but the beard is sparse. The abdomen is obese, with bluish striae. Brownish discolorations are present on both shins. The genitalia are small. The voice is high pitched. The heart is slightly enlarged to the left, and a systolic murmur is heard over the precordium. The blood pressure is 170 systolic and 120 diastolic. The electrocardiogram shows deviation of the axis to the left. The visual fields show no constriction.

A blood count showed 124 per cent hemoglobin, 5,580,000 erythrocytes and 11,700 leukocytes, with 61 per cent polymorphonuclear neutrophils, 33 per cent lymphocytes, 5 per cent monocytes and 1 per cent basophils. The Wassermann and the Kahn test were negative. A determination of the carbon dioxide of the plasma showed 72 cc. bound as bicarbonate per hundred cubic centimeters (normal 54 to 77 cc.). The whole chloride content was 455 mg. (as sodium chloride) (normal 450 to 500 mg.); the nonprotein nitrogen content 32.4 mg. (normal 25 to 30), and the cholesterol content 176 mg. (normal 150 to 180 mg.) per hundred cubic centimeters. The total protein content of the serum was 6.21 per cent (normal 7.4 per cent), the albumin being 4.42 per cent (normal 4.6 per cent) and the globulin 1.79 per cent (normal 2 per cent). The albumin-globulin ratio was 2.46. The calcium content of the serum was 10.8 mg. (normal 10 to 12 mg.) and the phosphorus content 3.62 mg. (normal 4 mg.) per hundred cubic centimeters. The phosphatase was 3.5 Bodanski units (normal 2 to 5 units). The curve of values for blood sugar in the dextrose tolerance test showed a rise to 245 mg. per

hundred cubic centimeters after one hour; at three hours the level was 84 mg. There were no abnormalities in the urine, and the test of renal function showed 75 per cent excretion of dye in two hours (normal 65 to 80 per cent).

Roentgen studies of the spine showed definite osteoporosis of all bodies of the vertebrae and ribs. Kyphosis was developing in the thoracic portion of the spine. Fractures of the second right and the eighth left rib were demonstrated.

DISCUSSION OF CASES OF CUSHING'S SYNDROME

DR. WILLIAM H. GOECKERMAN, Los Angeles: One often sees much more pronounced changes in the skin than these patients show. In every case I have observed in the past there has been a peculiar dusky appearance, usually associated with an acneform eruption, in addition to the changes noted in these cases.

DR. G. V. KULCHAR, San Francisco: The pictures presented by the 2 young men were typical of Cushing's syndrome. I could not see any typical striae in the woman. The evidence for this diagnosis was less definite in her case.

DR. FRANCES TORREY, San Francisco: All 3 patients have the same physical signs to a remarkable extent. The woman and the older boy have marked pigmentation and atrophic scarring of the legs. This is not unusual in Cushing's disease. The woman has definite striae on the upper parts of the arms and the abdomen, as have the other 2 patients. They all have high blood pressure and kyphosis. There has been no definite proof of pituitary adenoma or adrenal tumor in any case. I believe the adenoma of the pituitary can be small, however. In only a few of the cases recorded has there been definitely proved adenoma.

A Case for Diagnosis (Scleroderma?). Presented by DR. H. J. TEMPLETON, Oakland, Calif.

S. B. F., an oral surgeon aged 43, consulted me in August 1937 because of a peculiar, partially depigmented area of superficial atrophy over the right malar region and on the right side of the nose. There was no palpable hardening of the skin, nor had there been any. The process had gradually become apparent over approximately a year.

The diagnoses which were considered were idiopathic atrophy and scleroderma. Because of the question of a trophic basis, the patient was referred to a neurologist, who found no neural changes. He suggested that since the patient is an ardent trapshooter the repeated "kick" of a shotgun might have been partially responsible for the cutaneous changes. The basal metabolic rate was normal.

DISCUSSION

DR. L. R. TAUSSIG, San Francisco: I have no diagnosis to offer. The idea that the condition was caused by his shotgun seems a little far fetched to me. In shooting a shotgun the person receives the impact on the jaw, not as high up as this lesion.

DR. SAMUEL AYRES JR., Los Angeles: I think there is a little induration in the affected area, compared with the rest of the face, and superficial atrophy; around the border there is insignificant roughness of the skin, almost a slight stippling. I think the picture is suggestive of morphea.

DR. G. V. KULCHAR, San Francisco: I agree with Dr. Ayres. I believe that on palpation I could feel definite infiltration at the lower border.

DR. H. E. MILLER, San Francisco: When I saw this patient several months ago, I thought there was a blue tinge at the periphery of the area, suggesting scleroderma. I feel certain that there is some atrophy.

A Case for Diagnosis (Scleroderma? Lupus Erythematosus? Raynaud's Disease?). Presented by DR. L. R. TAUSSIG, San Francisco.

D. S., a woman aged 28, entered the University of California Hospital several weeks ago. Five years ago she had perforation of the bowel and later decom-

pensation with ascites. Two years ago she had redness and pain of her joints. Nine months ago for about three weeks she had swelling and stiffness of the joints of both upper and lower extremities and white scaly plaques over the elbows and the ears, and attacks of coldness and blanching of the fingers occurred about three times a day. These were almost always precipitated by exposure to cold and would persist until heat was applied. The fingers became swollen at this time and have remained so ever since. During the past three years, on four occasions, each lasting about a week, the patient has had flushing of the cheeks. This has not, however, involved the nose, to give a true "butterfly" distribution.

At present distal to the wrist and the knee the extremities are mottled blue, cold and clammy and blanch under pressure. Scattered diffusely but symmetrically over these areas are white atrophic patches and other areas in various stages of depigmentation. The most recent are pearl colored, slightly raised, firm, shiny, nontender and well demarcated. They occur on the palms as well as on the arms and the legs.

The lungs are clear. The heart is moderately enlarged. There is a gallop rhythm. Systolic and presystolic murmurs are heard at the apex.

The ascorbic acid content was low—0.23 mg. per hundred cubic centimeters. The urine showed a faint trace of albumin and 1 or 2 granular casts per high power dry field. The test of renal function with phenolsulfonphthalein showed 50 per cent excretion in two hours.

Sections from three biopsy specimens taken from the extremities were reported as showing chronic proliferative periarteritis and endarteritis.

DISCUSSION

Dr. Harry E. Alderson, San Francisco: This patient has severe circulatory disturbances. I should like to know whether any of the angular white scarlike artificial-looking lesions on her body are out of reach of her hands. These lesions strongly suggested artefacts to me.

Dr. William H. Goeckerman, Los Angeles: A picture of this type always puts one in a speculative mood. In an attempt to correlate this whole picture I shall suggest that this patient has the vasomotor type of scleroderma, with the scleroderma not as yet marked, and I should call the white spots on the right elbow lichen albus or lichen sclerosus et atrophicus.

Dr. Stuart C. Way, San Francisco: This woman says that the condition improves during the summer. Perhaps a part of the condition of her skin should be considered as pernio.

Dr. C. J. Lunsford, Oakland, Calif.: An edematous slightly infiltrated area is developing on the right side of the woman's face. I think that this, with the sclerodactylia, establishes the diagnosis of scleroderma.

A Case for Diagnosis (Panniculitis?). Presented by Dr. Harry E. Alderson and Dr. A. E. Ingels, San Francisco.

L. P., a woman aged 38, was first seen on Jan. 26, 1938. She complained that for eight months she had noticed that she "bruised easily"—that ecchymoses developed, rapidly enlarged and became hard. She was born in Italy but has lived in San Jose, Calif., for twenty-five years. She has three healthy children, aged 12, 17 and 19. She has contributed to the support of her family by working irregularly in canneries. She has always been nervous, excitable and prone to worry. Her diet for years has consisted mainly of spaghetti and cheese, with green vegetables and fresh meat rarely and fresh milk never. She was operated on in 1923 for a large hepatic abscess. For the past eight months she has been subject to weekly attacks of sour eructations, nausea and vomiting of bitter greenish fluid. During this time she has had nocturia (having to urinate 3 or 4 times nightly). About once a day burning and itching begin in the epigastrium, radiate quickly to her back and then spread over the body. These attacks last over an hour.

The cutaneous lesions are all said to have followed some sort of trauma. They are present on the posterior aspect of the right arm and of both thighs and buttocks. They appear as numerous slightly pigmented, firm, irregularly nodular, well circumscribed masses, adhere to the skin and extend into the subcutaneous tissue.

The patient has not received insulin, camphor liniment or other medication by injection.

General physical examination reveals nothing significant. Laboratory examinations of the blood, the urine and the stool showed nothing abnormal. Roentgenograms of the chest showed no abnormality. Roentgenograms of the lesion on the right arm made by Dr. Robert R. Newell, of San Francisco, with special attention to the soft tissues showed "plaques of induration with a definite increase in subcutaneous trabeculation in places."

Sections of biopsy material were presented.

DISCUSSION

Dr. A. E. Ingels, San Francisco: The sections showed inflammatory changes deep in the cutis. The fat-stained section testified that fat tissue had been absorbed, leaving fat-free lacuna. There was infiltration of round cells, young connective tissue cells, endothelial cells and plasma cells, and there were many giant cells. Endarteritis was present. No abscess formation was seen. This picture may fit in with a number of diseases that affect the lipoid tissue. Christian's disease might be considered. In this case, however, there has been no fever. Necrobiosis lipoidica diabeticorum is a possibility. Recently A. B. S. Bruce-Jones (*Brit. J. Dermat.* **49**:238 [May] 1937) reported 2 cases in which the findings were similar to those in the present case, except that there was no increase in the blood sugar. He expressed the belief that the condition may have different etiologic factors, among which diabetes is only one. Simple scleroderma was offered as a diagnosis but is untenable, both clinically and histologically. Traumatic panniculitis has been seriously considered.

Dr. H. J. Templeton, Oakland, Calif.: I should like to ask whether the microscopic picture rules out a Darier-Roussy type of sarcoid.

Dr. A. E. Ingels, San Francisco: Absolutely. There is no tubercle formation.

Dr. Nelson Paul Anderson, Los Angeles: I feel that this condition belongs in the group of traumatic or foreign body panniculitis. In that disease atrophy may not appear for several years after the original insult. The giant cells seen microscopically seem to indicate either a fat necrosis or a foreign body reaction to some substance injected at the time of the patient's severe illness several years ago.

Dr. Howard Morrow, San Francisco: I agree with everything Dr. Anderson has said.

Dr. Harry E. Alderson, San Francisco: The lesion on her arm is said to have followed a severe pinch which bruised this area. Those on the posterior aspect of her thigh occur in areas injured by the edge of the bench on which she sits at the cannery where she works. The picture is that of deep panniculitis. Repeated questioning has failed to reveal a history of any injections.

Dr. Merlin Trevor-Roper Maynard, San Jose, Calif.: I think that trauma is the main factor in the production of the lesions.

Dr. A. E. Ingels, San Francisco: As far as trauma is concerned, the lesions extend medially on the thigh, beyond where one would expect her to injure herself by sitting. The history of having been pinched once in the arm could hardly explain the extensive and progressive panniculitis seen in this area.

Rhinoscleroma. Presented by Dr. J. M. Graves, San Francisco.

T. P. G., a Central American aged 27, was previously presented at the meeting of the San Francisco Dermatological Society on Dec. 4, 1936 (Arch. Dermat. & Syph. **36**:1241 [Dec.] 1937).

Subsequently a bacillus belonging to the Friedländer group was cultured. This bacillus had the characteristics of the bacillus of Frisch. An autogenous vaccine was prepared from this culture, and from Jan. 7 to March 31, 1937, the patient received injections of 1 cc. every three to five days. From May 10 to June 24, 1937, the patient received weekly fever treatments (blanket method). The temperature averaged 105.8 F. for five hours. There was no essential change in the patient's condition. On June 30, 1937, roentgen therapy was started. A total of 1,200 r was administered, treatments being given on June 30, July 21, August 11 and October 1.

DISCUSSION

DR. HARRY E. ALBERSON, San Francisco: The picture is typical. The oral lesions often cause separation and eventual loss of the upper teeth. Dr. Kulchar has suggested that medication with sulfanilamide be tried.

DR. G. V. KULCHAR, San Francisco: This suggestion was simply a guess, based on the fact that the Frisch and the Friedländer bacillus are of the same group. Sulfanilamide has been used successfully in the treatment of pneumonia due to the Friedländer bacillus. If favorable results were likely to follow sulfanilamide therapy, they would probably appear in a short time.

DR. O. P. DIEDERICH, Fresno, Calif.: I tried sulfanilamide in 1 case of rhinoscleroma, and there was some improvement at first, but later the improvement was negligible. Some decrease in the size of the nodules was apparent.

Xanthelasma. Presented by DR. E. A. LEVIN, San Francisco.

G. S., a white man aged 39, was first seen in the University of California dermatologic clinic in September 1937. He had been under observation and treatment in the medical clinic because of a gastrointestinal complaint since April 1935. A diagnosis of cholecystitis was made at this time but was not confirmed by cholecystographic study. Duodenal ulcer with marked spasm and retention was diagnosed from roentgen study of the gastrointestinal tract in May 1936. The patient was then given a Sippy diet and other therapy for ulcers; this treatment was continued in a modified form until May 1937. The xanthomatous lesions, which began about November 1936, were first noted during a physical examination in May 1937.

At that time the yellowish orange deposits were extensive on both palms and in the webs of the fingers and the toes. There were groups of small nodules on the elbows and a few on the knees and scattered over the body. Severe daily headaches began about the time the xanthomas were first noted; these lasted from a few hours to a whole day. Physical examination, laboratory tests and roentgen study have shown no abnormality except for the cholesterol content of the blood. This was as follows:

	Mg. per 100 Cc.
Sept. 1937	695
Nov. 1937	498
Jan. 1938	666
Feb. 1938	695

The value for blood sugar during fasting on Sept. 14, 1937, was 95 mg. and in February 1938 93 mg. per hundred cubic centimeters.

On Feb. 3, 1938, the rose bengal test showed results within the limits of normal: at eight minutes, 50 per cent, and at sixteen minutes, 31 per cent.

On Feb. 3, 1938, the basal metabolic rate was —7 per cent.

In September 1937 a diet low in cholesterol was given.

Lichen Nitidus. Presented by DR. N. N. EPSTEIN and DR. E. A. LEVIN, San Francisco.

E. H., a white man aged 26, first noticed small smooth papules on the glans penis and the prepuce about one year ago. The lesions are asymptomatic and

are confined to those areas. They are slightly violaceous and glistening, sharply defined, polygonal and slightly raised above the level of the skin. There are about thirty or forty individual papules without any tendency to coalesce.

Biopsy of a specimen from one of the papules showed an atrophic epithelium, beneath which there was a circumscribed cellular infiltrate, chiefly in the papillary and the subpapillary layer. This infiltrate consisted of small round cells, epithelioid cells and a few giant cells.

DISCUSSION

DR. N. N. EPSTEIN, San Francisco: I think the striking thing about this condition is the amount of infiltrate seen microscopically in proportion to the clinical appearance of the lesion which is insignificant and easily overlooked. The pathologic picture was characteristic of lichen nitidus.

Parapsoriasis. Presented by DR. N. N. EPSTEIN, San Francisco.

J. R., a white girl aged 9 years, was first seen in the University of California dermatologic clinic on Jan. 25, 1938. An eruption consisting of sharply circumscribed plaques, which were superficial, nonindurated, fawn colored to erythematous and covered with small, somewhat adherent scales and varied from about 2 to 6 cm. in diameter had been present for eighteen months. There were no signs of excoriation, and the eruption was said to be only slightly pruritic. The plaques were scattered bilaterally over the body and extremities. Two areas about 9 cm. in diameter were symmetrically located, one on each side of the neck; these extended to the ears. There were no others on the face or the scalp and no lesions on the toes.

Physical examination and laboratory study showed no abnormality.

A biopsy specimen from a lesion on the thigh showed histologic changes compatible with parapsoriasis.

Parapsoriasis. Presented by DR. C. J. LUNSFORD, Oakland, Calif.

M. T., a man aged 20 years, was first seen in 1935 at the E. V. Cowell Memorial Hospital, Berkeley, Calif. A chronic macular scaly eruption is limited to his trunk and appears to follow the lines of cleavage of the body. There is no demonstrable atrophy. The eruption is generalized. There was at no time any erythema. There are no subjective symptoms. Scales from the lesions repeatedly showed no signs of Microsporon furfur. All laboratory procedures gave normal results; aside from a basal metabolic rate of —10 per cent. On several occasions the condition has improved temporarily under peeling exposures to radiation from a quartz lamp. He was presented before the San Francisco Dermatological Society two years ago. The majority of opinions supported the diagnosis of parapsoriasis.

During the last month a complete investigation by a responsible internist in Oakland, Calif, showed no abnormality except a basal metabolic rate of —20 per cent.

The eruption was not changed during the last two years except to extend a bit.

DISCUSSION OF CASES OF PARAPSORIASIS

DR. CHARLES R. CASKEY, Los Angeles: I agree with the diagnosis in the case of the young man, but in the case of the little girl it seems to me that further search for fungi should be carried out. Only two attempts have been made to culture the organism.

DR. SAMUEL AYRES JR., Los Angeles: I agree with the diagnosis in the case of the girl but not in that of the young man. The young man's lesions look like tinea versicolor.

DR. STANLEY CHAMBERS, Los Angeles: I am positive that the condition is tinea versicolor.

DR. H. E. MILLER, San Francisco: I also think it is tinea versicolor. I personally have examined scrapings from the lesions; I did not observe any organisms, however.

DR. H. J. TEMPLETON, Oakland, Calif.: I have watched the little girl about a year and have seen the lesions develop. I have not been convinced that the condition is parapsoriasis. The thing that worries me is that it might be an early stage of one of the lymphoblastomas, perhaps of mycosis fungoides.

DR. KENDAL FROST, Los Angeles: I agree with the diagnosis of parapsoriasis in both cases. The lesions in the man remind me of the condition of 2 sisters who were presented before the Los Angeles Dermatological Society with a diagnosis of pseudoatrophoderma colli, which was described by S. W. Becker and K. B. Muir (ARCH. DERMAT. & SYPH. **29**:53 [Jan.] 1934). The histologic changes were similar to those of parapsoriasis, and pseudoatrophoderma colli may turn out to be a variant of parapsoriasis.

DR. G. V. KULCHAR, San Francisco: I think that the man's condition is typical parapsoriasis of the Juliusberg type. As to the girl's condition, lesions of the en plaques type are usually yellow. Her condition may fall into the group of psoriasoid lesions.

DR. NELSON PAUL ANDERSON, Los Angeles: The rapid development of the girl's lesions, the fact that she does not look at all well and the microscopic picture suggest some type of lymphoblastoma. The microscopic section, while not allowing a positive diagnosis of lymphoblastoma, showed much more cellular infiltrate than occurs in ordinary parapsoriasis. The condition may subsequently prove to be mycosis fungoides. I suggest applying ½ skin unit of roentgen rays to one of the lesions to see what effect that would have on them.

Early Mycosis Fungoides. Presented by DR. G. V. KULCHAR, San Francisco.

H. W., a white woman aged 47, states that a generalized pruritic eruption began eight years ago and has persisted to the present time with periods of partial remission. Four years ago the diagnosis of mycosis fungoides was made at the Mayo Clinic. The patient has had generalized exposures to roentgen rays and fever therapy (diathermy), and chaulmoogra oil has been administered. There has been no improvement. No tumors have been present at any time.

Physical examination shows no abnormality except the condition of the skin. There is no generalized adenopathy. There is a generalized erythematosquamous eruption in the form of irregularly outlined plaques, with varying degrees of infiltration involving the trunk and to a less degree the face and the neck.

The basal metabolic rate was +1 per cent.

Sections of tissue were examined by Dr. A. E. Ingels, who reported: "considerable hyperkeratosis and a moderate amount of acanthosis. The cutis showed a relatively narrow zone of round cell infiltrate involving the papillary bodies and the upper part of the cutis. The cells showed a great variation in type and size. Some of them appeared immature and showed a tendency to clumping. There was some perivascular infiltration. The microscopic picture was considered compatible with that of early mycosis fungoides."

DISCUSSION

DR. N. N. EPSTEIN, San Francisco: I saw this patient eight years ago, when the condition first began. As I recall, it has not changed a great deal. If a diagnosis is to be made, I should prefer simply to place the condition in the lymphoblastoma group rather than definitely to put it into the class of mycosis fungoides.

Dr. A. E. INGELS, San Francisco: I agree with Dr. Epstein. In such cases Dr. Hamilton Montgomery designates the condition as malignant erythroderma, rather than atttempting to classify it definitely as leukemia, mycosis fungoides or some other specific condition.

Keratosis Follicularis. Presented by Dr. Orland F. Montgomery, San Francisco.

T. A., an Italian man aged 37, noticed elevations behind the ears, some of which contained pus, in 1919, while he was in the Italian army. The eruption has progressed until the entire face, the neck, the intrascapular and the intermammary region and the sides of the trunk are involved.

The primary lesion consists of a brownish papule about an individual follicle. Coalescence of these lesions forms solid patches between the shoulders and on the face and neck. There are vegetating lesions behind the ears. There are practically no subjective symptoms.

DISCUSSION

Dr. C. E. Schoff, Sacramento, Calif.: I agree with the diagnosis.

Dr. H. J. Templeton, Oakland, Calif.: I happened to run across a therapeutic suggestion in the Yearbook (Wise, F., and Sulzberger, M. B.: Yearbook of Dermatology and Syphilology, Chicago, The Yearbook Publishing Company, Inc., 1936). Recovery from Darier's disease was reported after injections of a gold preparation.

Dr. Orland F. Montgomery, San Francisco: Roentgen treatments have helped this patient considerably.

Dr. Kendal Frost, Los Angeles: I reported a group of cases of this disease a few years ago. In 1 case a series of injections of a gold preparation had been given without results.

Cutis Elastica Abnormally Sensitive to Trauma. Presented by Dr. J. D. Viecelli, San Francisco.

R. B., a white youth aged 18, complains that his skin is loose and that slight trauma produces thin atrophic scars. This has been noted since early infancy. The looseness of the skin increases peripherally, so that it is most noticeable on the extremities, where there are numerous irregularly shaped atrophic scars. Cutaneous pads are present over the joints of the fingers and toes. Blows of moderate intensity cause deep lacerated cuts, which heal readily when sutured and leave atrophic scars.

The patient is the eighth and last child in his family. His father died from cancer of the esophagus. His mother, sisters and brothers are all living and well. None have any evidence of a similar cutaneous anomaly.

Except for the appearance of a large abscess in the right lumbar region a number of years ago, he has been and is in excellent health. Two upper incisors are either lacking or unerupted, and the nails are rather thin and small. The hair is fine but of normal growth and distribution.

DISCUSSION

Dr. H. J. Templeton, Oakland, Calif.: I agree with the diagnosis but believe that the condition may be classified further as an example of the Ehlers-Danlos syndrome, which includes (1) a skin almost as fragile as that in epidermolysis bullosa, (2) cutis elastica and (3) hypermobility of the joints.

Dr. J. D. Viecelli, San Francisco: There have been no bullae. The patient is seeking advice because the condition of his skin forces him to restrict his activities.

Hereditary Hemorrhagic Telangiectasia (Osler). Presented by Dr. H. J. Templeton, Oakland, Calif.

H. D. S., a man aged 26, a student of the University of California, was presented before the San Francisco Dermatological Society on Sept. 27, 1935 (Arch. Dermat. & Syph. **34**:143 [July] 1936).

Although he has suffered from nosebleed for many years, only during the last four years has this been sufficiently serious to render him weak and anemic.

He has had to have the epistaxis controlled on numerous occasions by actual cautery. He has recently passed through a period of rather severe bleeding, after which a blood count showed 45 per cent hemoglobin and 3,910,000 erythrocytes. The rest of the blood count, including a platelet count, and determinations of coagulation and of bleeding time showed no abnormality.

Injections of moccasin venom were begun about one week ago. Although periodic bleeding still continues, the patient is under the impression that the bleeding stops more rapidly than it did. The bleeding time has decreased from four minutes to one minute.

DISCUSSION

DR. H. J. TEMPLETON, Oakland, Calif.: Fortunately the patient's father, whom I had not seen before, brought him in. He shows the same condition on his lips.

Fixed Eruption Following Injections of Neoarsphenamine. Presented by DR. C. J. LUNSFORD, Oakland, Calif.

C. L. T., a man aged 35, was seen by me a year ago because of a well circumscribed eczematoid eruption on the right palm, which showed superficial ulceration. The Wassermann reaction proved to be positive. He was referred back to his original physician for treatment and was not seen by me again until Feb. 11, 1938, at which time an eruption characterized by hyperpigmentation was present, predominantly on the buttocks and the upper parts of the thighs but occurring also on the feet, the fingers and the arms.

The patient states that after the third injection of neoarsphenamine one year ago dermatitis developed at the sites of the present pigmentation. This finally disappeared, presumably under the influence of sodium thiosulfate. The patient states that he has received alternate series of injections of a bismuth preparation and neoarsphenamine since and that after each series of injections of neoarsphenamine dermatitis has developed, always in the same location and always resulting in hyperpigmentation of the areas involved. There is no other history of ingestion of drugs.

DISCUSSION

DR. ERNEST K. STRATTON, San Francisco: I do not doubt that this fixed eruption is due to neoarsphenamine; however, when I questioned him the patient stated that he has taken a drug containing phenolphthalein occasionally as a laxative. When the eruption clears, I should like to see a therapeutic test made with phenolphthalein.

DR. C. J. LUNSFORD, Oakland, Calif.: This is interesting additional history that I did not obtain. I shall follow Dr. Stratton's suggestion.

DR. N. N. EPSTEIN, San Francisco: The flare-up of these lesions after the use of neoarsphenamine can hardly be disregarded as a factor.

Coccidioidal Granuloma. Presented by DR. H. E. MILLER, San Francisco.

A. J. R., a man aged 40, was previously presented before the San Francisco Dermatological Society on Dec. 4, 1936 (ARCH. DERMAT. & SYPH. **36**:1240 [Dec.] 1937). At that time he presented an unusual picture of coccidioidal granuloma characterized by a brawny induration and erythema of the nose, the upper lip and the cheeks. This began as a "pimple" in 1934. Subsequently the patient was given 0.25 Gm. of calcium creosotate every two hours for eight doses each day. No improvement was noticeable after one month. Roentgen therapy was then instituted. From Dec. 18, 1936, to Feb. 2, 1937, the patient received a total of 950 r, with some benefit. On March 30, 1937, intradermal and subcutaneous injections of coccidioidal vaccine were begun and continued at three or four day intervals until June 1937. During this time there was slight improvement. The patient has returned for observation at six week intervals for the last six months. There has been little change in his appearance except for a slight

decrease in the edema of the upper part of the face. A roentgenogram of the chest taken in January 1938 showed no change.

DISCUSSION

DR. MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif.: I saw this man early in 1934. At that time there were verrucous lesions and erythema around the alae of the nose. I made a diagnosis of erysipelas perstans faciei of Kaposi. Later, on the basis of the microscopic picture, a diagnosis of tuberculosis cutis was made.

DR. SAMUEL AYRES JR., Los Angeles: Has this patient's condition progressed under treatment?

DR. H. E. MILLER, San Francisco: The man has had considerably more edema and redness of the face in the past several months than when Dr. Maynard first saw him. This was markedly improved for a while and only recently has recurred. The improvement was undoubtedly due to roentgen treatment.

Blastomycosis. Presented by DR. F. G. NOVY JR., Oakland, Calif.

J. R., a white man aged 40, was first seen in the University of California dermatologic clinic on July 21, 1937. He had had urinary difficulty for three years, and there was acute retention on the day of entry. For three years there had been dyspnea and orthopnea. A loss of 40 pounds (18 Kg.) had occurred in the last two years. For the last six months he had suffered from articular pains, abdominal distress and general malaise. Ten weeks before his entry subcutaneous swelling had appeared on the right hand, the elbow and the lateral aspects of both thighs.

Examination shows ten cutaneous lesions ranging from 2 to 5 cm. in diameter scattered widely over the body. They are in various stages of ulceration, crusting and healing. The more active lesions are fungating masses which discharge purulent material through multiple peripheral sinuses. Active lesions are to be seen on the dorsum of the right hand, above the right elbow and on the lateral aspects of both thighs.

The blood pressure was 210 systolic and 110 diastolic. The heart was slightly enlarged to the left. The peripheral vessels were moderately sclerotic. The prostate was enlarged to two or three times normal size and was hard.

Round budding organisms were demonstrated in the exudate taken from the cutaneous lesions. Later, the same budding organisms were demonstrated in the sputum and in a catheterized specimen of urine.

Cutaneous tests with coccidioidin gave negative results.

Culture of exudate from the skin produced a downy white filamentous fungus.

Results of microscopic examination of sections from a lesion on July 24, 1937, were reported as follows: "The dermis was thickly infiltrated by polymorphonuclear leukocytes and eosinophils and many giant cells. Scattered in the densely infiltrated and fibrotic tissue were round clear double-coated neutral-staining bodies, one of which appeared to be budding." The diagnosis was blastomycosis of the skin and subcutaneous tissue.

A roentgenogram of the chest revealed a feathery increase in all pulmonary markings and confluent infiltration in the upper third of each lung with cavitation. Blastomycosis or bilateral tuberculosis was considered most likely.

Roentgenograms of the spine showed no evidence of involvement, but intravenous pyelographic study revealed a suggestive filling defect in the right renal pelvis.

The Wassermann and the Kahn test were negative.

A blood count revealed 90 per cent hemoglobin, 5,400,000 red blood cells and 13,200 white blood cells, with a differential count of 78 per cent polymorphonuclears, 18 per cent lymphocytes and 4 per cent monocytes.

A retention catheter was necessary during the patient's entire stay in the hospital.

He was given roentgen therapy (1,050 r divided into ten doses to the prostate and 150 r with 0.1 mm. aluminum filter to a lesion on the right thigh) and massive doses of sodium iodide.

The patient was discharged from the hospital on September 15 and reentered on November 9 for transurethral resection. Microscopic examination of tissue removed at the operation showed "chronic granuloma of the prostate." The lesion on the right thigh had regressed to a pigmented scar.

On Jan. 4, 1938, another course of roentgen radiation to the lesion over the dorsum of the hand, which had remained granulomatous, was begun.

DISCUSSION

DR. R. A. STEWART, San Francisco (by invitation): This condition is blastomycosis with unusually extensive systemic involvement. It improved for a while during the administration of iodides, but later the lesions flared up.

A Case for Diagnosis (Tuberculosis Verrucosa Cutis?). Presented by DR. FRANCES TORREY, San Francisco.

E. D. P., a woman aged 21, was first seen in the University of California dermatologic clinic on Dec. 2, 1937, because of a lesion that had been present on the dorsum of her left hand since she was 2 years of age. At present the lesion consists of a fungating granulomatous area covering most of the second and third metacarpal bones and extending onto the proximal phalanx of the index finger. The middle finger has already been amputated because of its involvement by this process.

She has scarring on both corneas, and a consultation with the ophthalmologic department brought fourth the opinion that this was characteristic of old interstitial keratitis, probably on the basis of congential syphilis, although there were no other physical or laboratory signs of this.

Cultures showed no fungi. Material from the lesion was inoculated into a guinea pig, which has so far remained well. Microscopic sections showed chronic granuloma.

DISCUSSION

DR. H. E. MILLER, San Francisco: When I first saw this patient, I made a tentative clinical diagnosis of tuberculosis verrucosa cutis. Blastomycosis was considered, but that diagnosis did not seem to be compatible with the long duration and the localization of the disease. The results of autopsy of the inoculated guinea pig may solve the problem.

DR. WILLIAM H. GOECKERMAN, Los Angeles: In the treatment of blastomycosis it is a common practice to give fractional doses of roentgen rays, ¼ skin unit once a week. My experience has been that it is better to give a ¾ skin unit dose less frequently. Even tuberculosis verrucosa cutis does much better under this dosage. In the Middle West, there formerly were many cases of blastomycosis and later only an occasional one. I wonder why that was.

DR. G. V. KULCHAR, San Francisco: The lesion seemed rather moist for one of tuberculosis verrucosa cutis, although cutaneous tuberculosis of this type may occasionally be purulent. I suggest a possible diagnosis of pseudoblastomycetic pyoderma. In a case I presented at the Sept. 18, 1936, meeting of the San Francisco Dermatological Society (ARCH. DERMAT. & SYPH. **36**:659 [Sept.] 1937) some improvement followed applications of zinc peroxide. I saw the patient again last week, when he had a recurrence.

DR. MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif.: I asked the patient about the site of the biopsy specimen, and she said it was taken from the center of the lesion. I suggest that a specimen be taken from the border.

DR. R. A. STEWART, San Francisco (by invitation): One specimen was taken from the center and one from the edge.

DR. NELSON PAUL ANDERSON, Los Angeles: I think this case is one of tuberculosis verrucosa cutis. I believe that the patient had spina ventosa, which is tuberculosis of the bone, involving one of the phalanges. I think that the process in the skin is secondary to this. As therapy I suggest actual cautery or excision. I do not believe that roentgen therapy will ever heal the condition.

Lupus Pernio. Presented by DR. ERVIN EPSTEIN, Oakland, Calif.

A. W., a white man aged 23, stated that adenopathy developed on the left side of the neck during the winter of 1934. This was proved to be tuberculous by histologic studies and by inoculation of a guinea pig. A tuberculin test at this time gave a positive result. Repeated fluoroscopic and roentgen examinations have failed to reveal any pathologic changes in the lungs. A recent roentgen study showed that there were no fibrocystic changes in the hands. The patient has been treated for scrofula at the Arroyo Sanatorium, Livermore, Calif.

Soon after the appearance of the adenopathy the patient noticed that his ears became violaceous, a change which soon became permanent. Occasional necrotic papules appeared on the rims of the ears and on the dorsa of the hands. There have been numerous remissions and relapses during the last three years.

At present both ears are a dusky color but are not thickened. A necrotic area is present on the posterior rim of the left ear. There are no lesions on the hands. Therapy to date has included administration of a Sauerbuch-Herrmannsdorfer diet, ultraviolet radiation, cod liver oil by mouth and calcium gluconate intravenously. The last agent seems to have been the most beneficial to date.

DISCUSSION

(All the members agreed with the diagnosis.)

A Case for Diagnosis. Presented by DR. E. A. LEVIN, San Francisco.

M. L., a white woman aged 28, was first seen in the University of California dermatologic clinic in January 1938 because of atrophic areas of skin around the chin and the lips, more pronounced on the left side. These appear as small irregular shallow depressions. There is no discoloration or thickening of the skin. The patient complains of stiffness of the neck and jaw and occasional pain in the mandibular joints. There is marked sweating, confined to the right side of the face. The sweat appears in small drops and is accompanied with a decided flushing of the entire right side of the face. The patient has noticed this for two years. At first there was associated burning of the face and the inside of the mouth and pain in the jaws. For one year there has been a gradual decrease in the menstrual flow.

Physical examination in December 1937 showed no abnormality except a scar from thyroidectomy in 1932. A neurologic examination showed only diminished corneal reflexes.

The impression of the neurologic department is overactivity of the vegetative nervous system.

The visual fields are normal.

The basal metabolic rate was +6 per cent.

DISCUSSION

DR. NELSON PAUL ANDERSON, Los Angeles: Since there has been no inflammatory process around the mouth and chin, one ought to consider some type of vermiculate atrophy.

Multiple Hypertrophic Scars in a Child 4 Years Old. Presented by DR. HARRY E. ALDERSON, San Francisco (from the Department of Dermatology and Syphilology, the Stanford University School of Medicine).

This healthy 4 year old white girl, a native of San Salvador, whose features, like those of her mother, are of the Caucasian type, presents about eight typical

enormous keloidal scars on the upper parts of the shoulders, the arms and the lower part of the back. They resulted from burns when boiling hot soup was accidentally spilled on her about a year ago. The burns were promptly treated with trinitrophenol and paraffin, and she had good care by Dr. Esteban Reyes of El Salvador, who referred her to me.

My associates and I could obtain no history of Negro blood but were told that the paternal grandfather's brother had keloids.

Some of the scars have been removed surgically, and roentgen radiation was promptly applied. This did not prevent the recurrence of the keloids. Suggestions for treatment will be welcomed.

DISCUSSION

DR. A. E. INGELS, San Francisco: As regards roentgen therapy, I believe that a series of small fractional exposures are as good as larger single exposures. Her lesions have involuted considerably under weekly irradiation with 75 r without a filter. Eight treatments were given in one course, and the treatment was repeated after five or six weeks.

DR. CHARLES R. CASKEY, Los Angeles: I believe that in most cases keloid occurs in women. Why that is I do not know. I believe that improvement after roentgen treatments with only 75 r would probably be spontaneous improvement and that larger amounts would have to be given to influence the course.

DR. HOWARD MORROW, San Francisco: I think that this condition should be let alone.

Lupus Erythematosus. Presented by DR. H. J. TEMPLETON, Oakland, Calif.

L. H., a woman aged 33, came to the dermatologic clinic of the E. V. Cowell Memorial Hospital, Berkeley, Calif., in November 1937, because of a lesion on the lower lip, which had been present for about two years. It involved approximately two thirds of the vermilion border and the skin of the lower lip in an irregular bandlike area varying up to 7 or 8 mm. in width. It was dull red, scaling and superficially infiltrated. There was a difference of opinion as to the presence of follicular "plugging" and of early atrophy in the more marked areas. There was marked seborrhea of the scalp. The patient has no specific general complaints. She states that she tires easily and is subject to constipation. She is somewhat underweight and inclined to be nervous. There has been no recent illness.

The tuberculin test gave a positive result. There were scars of old tuberculous cervical lymphadenitis, active between the ages of 6 and 8 years. A roentgenogram of the chest showed signs of mild old tracheobronchial tuberculosis of the lymph nodes but no evidence of recent activity. Roentgenograms of the teeth revealed apical abscesses around several. Extraction of these was advised. The sedimentation rate, determined by the diagonal line method, was 13.5 mm. A blood count showed 74 per cent hemoglobin, 4,120,000 erythrocytes and 7,200 leukocytes, with 53 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 1 per cent basophils, 40 per cent lymphocytes and 4 per cent monocytes. The Wassermann reaction was negative. The urine was normal, and the stools showed no protozoa or worms. There is intercurrent herpes simplex on the left side of the lip today. The differential diagnosis rests between seborrheic eczema and lupus erythematosus.

DISCUSSION

DR. STUART C. WAY, San Francisco: This patient appears to me to have seborrheic eczema.

DR. MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif.: I think that if these lesions are examined closely under a diascope or with a magnifying glass there will not be much doubt that the condition is lupus erythematosus. The patient did have tuberculous glands in the neck as a child, so that tuberculosis might be an etiologic factor.

DR. SAMUEL AYRES JR., Los Angeles: I think the lesions on the lip are suggestive of lichen planus. There are a definite violaceous appearance and a slight tendency to umbilication. In one place there is white striation, which is suggestive of lichen planus of the lip.

DR. STANLEY CHAMBERS, Los Angeles: With the hand lens one can identify lesions characteristic of lupus erythematosus.

A Case for Diagnosis (Poikiloderma Atrophicans Vasculaire? Scleroderma?). Previously presented by DR. L. R. TAUSSIG, San Francisco.

Lichen Planus (New Lesions Appearing Where Adhesive Plaster Was Applied). Presented by DR. W. M. MEININGER, San Francisco (by invitation).

Lupus Erythematosus and/or Psoriasis. Previously presented by DR. H. J. TEMPLETON, Oakland, Calif.

Scleroderma. Presented by DR. L. R. TAUSSIG, San Francisco.

BRONX DERMATOLOGICAL SOCIETY

SAMUEL M. PECK, M.D., *Vice President, Presiding*

March 24, 1938

HENRY SILVER, M.D., *Secretary*

Macular Atrophy, Secondary to Syphilis. Presented by DR. SAMUEL FELDMAN.

N. B., a Negress aged 24, had a genital chancre in 1932. This was followed in about three weeks by a secondary eruption which involved mainly the trunk. The eruption cleared up in about two months, owing to mercury rubs. The patient received no other treatment until October 1936. At the Vanderbilt Clinic a Wassermann test gave a positive result. She was treated with neoarsphenamine and a bismuth preparation for five months and was transferred to the Morrisania Hospital. She states that the condition for which she is presented was not present before the syphilitic infection but followed directly after the disappearance of the secondary eruption.

The entire back is covered with numerous elevations, which range in size from that of a pinhead to that of a sago seed; few lesions are as large as a lentil. The elevated lesions have a flat and decidedly wrinkled surface, best seen when relaxation of the skin is produced by forcing the shoulders backward. Some of the smaller lesions show a central depression. The lesions tend to follow the natural lines of cleavage. In the lumbar region and on the buttocks the lesions are somewhat larger, slightly elevated and firm, with a smooth surface; a few lesions, however, show a wrinkled surface. On the front and the sides of the abdomen are numerous minute globular shiny papules.

Microscopic examination of a minute papule from the abdomen showed no changes other than an interstitial and parenchymatous edema of the collagen. Sections from a wrinkled papule and from a firm lesion showed thinning of the epidermis and flattening of the papillae. The cutis was markedly edematous. The collagen bundles were thick and less wavy than usual and stained rather poorly. The elastic tissue in places was diminished and broken up into small fragments and in other places was missing altogether. No blue-stained elastic tissue appeared with the orcein and polychrome methylene blue stain.

DISCUSSION

DR. HENRY SILVER: One is accustomed to a definite clinical picture when diagnosing atrophy or syphilitic macular atrophy. Almost always lesions show ballooning. Unless this is present it is difficult to diagnose macular atrophy on purely clinical grounds. The wrinkling shown by a number of lesions in Dr. Feldman's case cannot be regarded as characteristic of macular atrophy as it is observed in the end stage of many eruptions, among them lichen planus.

DR. DAVID L. SATENSTEIN: I do not like to disagree with Dr. Silver on the subject of macular atrophy, but I think this condition is a good example of punctate atrophy. The proof, however, that this atrophy followed a syphilitic eruption is up to the presenter. I recall a patient who had macular atrophy and syphilis, but the former condition did not follow in the wake of syphilis. I have observed many cases of macular atrophy in which ballooning was not present. The diagnosis of macular atrophy, besides its clinical grounds, is made with greater certainty on microscopic grounds. I think this case is remarkable —in fact, it is one of few that I have ever observed in which the lesions were of such a minute punctate type.

DR. LOUIS CHARGIN: I think this case is one of secondary macular atrophy, which I do not think resulted from a preceding syphilitic eruption. If syphilis had been the forerunner, it would have been of a follicular type, and the lesions would show a tendency to grouping not present in this case.

DR. SAMUEL FELDMAN: Herniation is not observed because the lesions are so small that the palpating finger cannot detect it. With regard to the question of syphilis, there is no way in which I can prove my contention. All I know is that the patient has syphilis, and according to her statement the lesions followed directly the disappearance of the secondary syphilitic eruption. At least she has had no other eruption since the secondary eruption.

Unusual Cutaneous Manifestations in a Psychopathic Patient (Malingering?). Presented by DR. HENRY SILVER.

L. B., a housewife aged 42, was first seen in September 1935 at the Bronx Hospital. She then presented raised various-sized fungating lesions on the back of the neck, the volar surfaces of the wrists, the fingers and the thighs. A tentative diagnosis of bromoderma was made, but a search for bromides gave negative results. On Feb. 25, 1936, the patient appeared at the Mount Sinai Hospital. She presented eroded and ulcerated lesions on the mucous membrane of the mouth. On the right buccal mucosa and underneath the tongue were flat ulcers the size of a nickel, with a grayish granular base and indurated sharp borders. It was difficult to fit these lesions into any known disease of the mouth. Cultures showed no organisms. The Wassermann test, urinalysis and routine and chemical examination of the blood showed no abnormality. Patch tests gave negative results. A culture of material from a lesion on the index finger showed no organisms. In a search for drugs, copies of prescriptions which had been given the patient were analyzed. The mixtures contained codeine sulfate, sodium salicylate, acetylsalicylic acid and acetophenetidin. Oral administration of these drugs gave negative results.

On Sept. 8, 1936, the patient was referred to the medical department for a thorough examination, which showed no essential abnormality. On Jan. 19, 1937, she presented a new crop of malodorous necrotic lesions on the sides of the tongue, the anterior pillars and the throat. The patient again claimed that the lesions followed a recent attack of grip. On Feb. 9, 1937, she was admitted to the hospital. The lesions healed rapidly, and she was discharged on Feb. 17, 1937.

In April 1937 she had a new crop of necrotic lesions of the mouth, which persisted for some time. The patient began to lose weight, because the painful lesions interfered with the intake of food.

In July 1937 she presented bullous lesions the size of a split pea or a lima bean, with an infiltrated red base involving the left thumb and the middle phalanx of the right index finger. The patient stated that she had taken no drugs at that time. Again a differential blood count and a chemical analysis of the blood showed no abnormality. Since then lesions have alternated at frequent intervals between the fingers and the mouth. At another hospital amputation of a finger was considered because of a deep gangrenous lesion.

In observation over two years various diagnoses have been suggested to correspond with the temporary clinical manifestations.

DISCUSSION

DR. HENRY SILVER: I can give only the highlights of this patient's voluminous record, which reads like a compendium of dermatology. Among diagnoses suggested have been drug eruption, moniliasis, Vincent's angina, pemphigus and syphilis. The psychopathic background of the patient was recognized early, but it was difficult to suspect a miserable little woman who evoked much sympathy, who was at times helpful and who sincerely sought medical aid. It became clear, in view of the variety of the bizarre clinical manifestations, the psychopathic background and the completely negative results of the thorough investigation, that the lesions were self inflicted.

A Case for Diagnosis (Pseudopelade of Brocq?). Presented by DR. ADOLPH ROSTENBERG.

This patient, a man aged 29, presents a condition of the scalp of two years' duration. It began in the occipital region and progressed slowly. Numerous round, oval or irregularly shaped bald areas all over the scalp range from ½ to 3 inches (1 to 8 cm.) in diameter. The skin is white, shiny and distinctly atrophic, with no evidence of pustules or horny plugs. There are no subjective symptoms except mild itching. The hair which is still present does not show any abnormality. There is a suggestion of lichen spinulosus around the left elbow. The Wassermann reaction was negative.

DISCUSSION

DR. SAMUEL FELDMAN: This boy was under my care for six months and only recently disappeared from my observation. When first examined, he presented definite folliculitis decalvans. Pustular follicular lesions cleared up under treatment. At present the condition seems quiescent, and no inflammatory lesions are in evidence. Little's disease should not be confused with this condition. Little found that his interpretation of the syndrome described by him was erroneous and that the disease has no relation to folliculitus decalvans.

DR. HENRY SILVER: Recently an excellent monograph on pseudopelade (Photinos, P. B.: La pseudo-pelade de Brocq, Paris, A. Maloine et fils, 1930) appeared from the laboratory of Sabouraud. In it the author established pseudopelade as a definite clinical entity by clinical and histologic studies.

DR. ADOLPH ROSTENBERG: The literature on the subject of pseudopelade and folliculitis decalvans is confusing. In my case no visible inflammatory process preceded the alopecia.

Pigmented Purpuric Lichenoid Dermatitis (Gougerot). Presented by DR. SAMUEL M. PECK.

C. B., a nurse aged 44, born in the United States, noted an eruption around the right ankle about a year ago. It gradually became more extensive, isolated spots appearing on the thighs and the elbows. The ankles become swollen after she stands for a few hours. There is slight itching. The patient is sensitive to morphine and takes a great deal of acetylsalicylic acid and aminopyrine for headaches.

On the dorsa of the feet, extending from a little above the ankles down to the toes, are irregular areas of an eruption of which the primary lesion is a purpuric spot or a purpuric lichenoid papule. Many of the papules are brownish; others show telangiectatic spots, while still others are red and cannot be made to disappear under pressure. These are evidently hemorrhagic. There is no particular tendency to form rings, but the papular and flat purpuric spots conglomerate to form patches of scaling and slight eczematization. Other patches are distinctly lichenified, and even in these areas there are scattered purpuric spots. As the older lesions undergo involution they become flat and somewhat scaly, but not atrophic, and instead of the red color of fresh hemorrhage show the yellowish picture of old dermatitis haemostatica. Over both external malleoli there are large scaly patches with marked infiltration and lichenification. The color is red, owing to diffuse cayenne pepper stippling. Scattered over the legs and on the thighs are small patches similar to those on the feet. There are no varicosities, but on the thighs and legs numerous dilated venules are seen.

Examination of the blood showed 97 per cent hemoglobin, 4,570,000 red cells and 5,600 white cells. The differential count showed 55 per cent polymorphonuclears, 43 per cent lymphocytes, 2 per cent monocytes and 150,000 platelets. The venom test gave a negative result.

Histologic examination of a recent lesion from the dorsum of the right foot showed hyperkeratosis, with a slight tendency to a parakeratotic scale. The epidermis was acanthotic in some areas and thin in others, especially where it was lifted up to form a papule by the underlying edema and inflammatory reaction in the papillary body. The basal cells showed intracellular edema. There was no spongiosis. There were several areas of fresh hemorrhage, especially in the edematous papillary body. In the upper part of the cutis were scattered areas of inflammatory reaction composed mainly of mononuclear cells. This infiltration seemed to center around blood vessels which, if one were to judge from the thickness of their walls, were small arterioles. Their walls were edematous, and the endothelial cells lining these blood vessels were swollen. While there was no real necrosis of the walls of the vessels, there seemed to be a tendency for degeneration, so that their outlines were faded and they stained poorly. There was a great deal of iron-containing pigment in the cutis.

Injections of venom were instituted on Jan. 17, 1938, and continued twice weekly. On March 22, 1938, there were no raised lesions, and the papular element had disappeared. Over the dorsum of the right ankle and around both external malleoli there are still dry red purpuric spots the size of a pinhead, with fading old hemorrhagic areas. The affected area gives the picture of an irregular stain about 4 cm. wide, made up of purpuric puncta and brownish red areas (older hemorrhages) with no definite scaling but a distinct feeling of roughness. The eczematoid lichenified part has practically disappeared.

DISCUSSION

DR. WILBERT SACHS: The clinical picture of the disease includes purpuric spots and papular lichenoid lesions. This picture does not resemble the original description or the picture in the case presented by F. Wise and J. Wolf (ARCH. DERMAT. & SYPH. **31**:445 [April] 1935). For instance, telangiectasia and pigmentation are entirely absent.

DR. ARTHUR SAYER: In the case of pigmented purpuric lichenoid dermatitis recorded by H. Gougerot and Paul Blum (*Bull. Soc. franç. de dermat. et syph.* **32**:161, 1925), there was definite pigmentation, and the lesions were most extensive on the legs and not present on the feet.

DR. SAMUEL M. PECK: I have always maintained that to be able to discuss purpuric hemorrhagic eruption of the skin one must have observed a great many related cases. Syndromes of this type have so many points in common that study of enough cases at one time might show those bearing different diagnoses to have a common etiologic background and merely to present varied pictures

of the same disease. If one examines patients with such conditions at various stages without knowing the whole background of the disease, it is easy to understand why one assumes that they have various dermatoses instead of the changing picture of a single disease.

A Case for Diagnosis (Seborrheic Eczema?). Presented by Dr. H. B. Feiler.

L. D., a presser aged 50, was seen at the Lebanon Hospital on March 8, 1938. He has a generalized eruption of four weeks' duration. On the forehead the eruption consists of reddish raised plaques which in some areas have become confluent. On the neck and in the groin the lesions are large, violaceous and sharply demarcated. The patient states that the lesions in the groin appeared first. In the axillas the lesions are reddish brown. On the chest some of the lesions appear to be clearing in the center and are slightly scaly, while on the back they are studded with small pustules and vesicles. The appearance of the various lesions has been modified by medication. Itching is not marked. The patient states that he had a similar eruption about a year ago, which cleared up in a short time under local treatment.

The hemoglobin content and the red and the white blood cell count were normal, as was the urine. The Wassermann reaction was negative.

DISCUSSION

Dr. Arthur Sayer: The scalp appears definitely seborrheic, and several plaques over the body appear clinically to be seborrheic eczema. However, the diagnosis of mycosis fungoides should be seriously considered, because of the peculiar character of the eruption on the sides of the neck and in the groins. In these locations there are large tumefied plaques, and such lesions are never seen in seborrheic eczema but are frequently observed in the lymphoblastomas, especially mycosis fungoides.

Dr. Samuel M. Peck: While I do not offer a definite diagnosis, the condition impresses me as having a parasitic background. The lesions suggest moniliids. They do not resemble mycosis fungoides, at least clinically.

Dr. Louis Chargin: The eruption on the scalp certainly suggests seborrheic eczema. The eruption on the arms and the trunk is difficult to diagnose. Dr. Sayer thinks it is mycosis fungoides, because there are a few tumefied lesions. These and the lesions resembling seborrheic eczema do not suffice to make a diagnosis of mycosis fungoides. I do not think that the lesions of the body are of parasitic origin. The eruption on the trunk is not typical seborrheic eczema but fits in best with that diagnosis.

A Case for Diagnosis (Lupus Erythematosus? Pseudopelade of Brocq?). Presented by Dr. Eugene F. Kelley.

M. N., a housewife aged 36, was first seen in the Department for Cutaneous Diseases of the Yonkers General Hospital, Yonkers, N. Y., on Dec. 13, 1937. On the vertex of the scalp is a roughly star-shaped slightly pink smooth shiny atrophic lesion. Toward the periphery several erythematous areas the size of a dime are covered with adherent dry white scales. No pustules, crusts or broken-off hairs have been present at any time. There is slight itching.

The Wassermann reaction was negative. Thirteen intramuscular injections of bismuth subsalicylate were given at weekly intervals; this resulted in diminution in the size and the number of the erythematous and scaly areas and in disappearance of the itching.

DISCUSSION

Dr. Charles Lerner: I prefer the diagnosis of pseudopelade of Brocq to that of lupus erythematosus. I was unable to discern patulous follicular orifices,

adherent scales or definite erythema. If this condition were lupus erythematosus, I think by this time there would be more atrophy. Perhaps another point against lupus erythematosus is the location of the lesions on the posterior part of the scalp rather than in the anterior regions.

DR. ARTHUR SAYER: Most patients with lupus erythematosus of such long duration as this would have had facial lesions at some time; this patient states that he has had none. I think that a biopsy will settle the diagnosis, because lupus erythematosus at this stage would show definite basophilic degeneration of the collagen bundles.

DR. DAVID L. SATENSTEIN: The erythema, the scaling and the surrounding atrophy favor the diagnosis of lupus erythematosus. The location of the lesions is of no importance.

DR. EUGENE F. KELLEY: When I first saw this patient, three months ago, the lesions were more erythematous and scaly. At that time I made a presumptive diagnosis of lupus erythematosus. There were no lesions on the glabrous skin. The response to bismuth therapy tends to confirm my first impression.

Lichen Planus; Secondary Syphilis. Presented by DR. LEO SPIEGEL.

I. G., a fireman aged 33, was presented at the March 1, 1938, meeting of the Section of Dermatology and Syphilis of the New York Academy of Medicine (this issue, p. 470).

DISCUSSION

DR. SAMUEL FELDMAN: I was interested in seeing this patient because I have reported cases of similar involvement several times. I have seen eruptions begin with lesions resembling pityriasis rosea but in a short time change their character until little by little, the true nature of lichen planus becomes evident. In this case the color of lichen planus is not present.

DR. DAVID L. SATENSTEIN: Did the presenter take into consideration the possibility that lesions resembling lichen planus can follow the ingestion of arsenic? I have seen that happen in a few cases.

DR. CHARLES WOLF: I am inclined to believe that this extensive eruption is probably caused by ingestion of drugs. When lichen planus is generalized as in this case, itching is usually a predominant symptom; that is not true in this case.

DR. WILBERT SACHS: This case is interesting because the histologic picture was not that of ordinary lichen planus, but there were areas suggesting bullous lichen planus as well as some evidence of retrogressing or atrophic lichen planus. I surmise that the biopsy specimen was taken from an annular lesion.

DR. ADOLPH ROSTENBERG. In a patient under my care a lichen planus-like eruption developed after an injection of arsphenamine and disappeared quickly after the arsphenamine was discontinued. With each new injection the eruption recurred. I think that if the eruption in this case were due to arsenic it would have cleared up by this time. I am, therefore, of the opinion that it is lichen planus.

DR. LEO SPIEGEL: Originally the diagnosis was pityriasis rosea in a syphilitic patient. It is evident this evening that the eruption is lichen planus which is responding to therapy.

Chancroids Cured with Sulfanilamide. Presented by DR. ADOLPH ROSTENBERG.

L. J., a Negro aged 35, was presented before this society at the February 1938 meeting (ARCH. DERMAT. & SYPH. **38**:130 [July] 1938).

DISCUSSION

DR. ADOLPH ROSTENBERG: For the past four months the patient was treated for chancroids by routine methods but failed to respond. After sulfanilamide

was administered, the response was dramatic. He received 120 grains (7.76 Gm.) of sulfanilamide, and the lesions and bubo cleared completely.

Dr. H. Victor Mendelsohn (by invitation): Can Dr. Chargin state whether sulfanilamide has been successfully employed in Negroes with a condition resembling granuloma inguinale and resistant to all forms of treatment?

Dr. Samuel M. Peck: Years ago Dr. Jerome Kingsbury and I (*J. A. M. A.* **87:**1900 [Dec. 4] 1926) reported good results in the treatment of phagedenic ulcers with antimony and potassium tartrate intravenously. This treatment was carried out twice weekly for three or four weeks. This form of therapy was greeted with great acclaim at that time and then for some reason fell into disuse.

Dr. Louis Chargin: I have seen patients with ulcers on the genitals which were not chancroids, and in these sulfanilamide therapy was unsuccessful. On the other hand, sulfanilamide has been successful in 24 out of 25 cases of chancroid.

Lupus Erythematosus. Presented by Dr. Charles Wolf.

J. W., aged 46, was presented before this society at the February 1938 meeting. During the past month new lesions have developed on the left side of the face; these are bullous and have an erythematous base.

DISCUSSION

Dr. David L. Satenstein: I should say the condition is a bullous type of lupus erythematosus. The pemphigoid type of lupus erythematosus develops rapidly, and the microscopic picture is that of an intense acute edematous process.